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SECTION OF CHEMICAL SCIENCES

ENVIRONMENTAL FACTORS IN STEREOREGULAR POLYMERIZATION*

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The discovery of catalytic systems capable of polymerizing ethylene to polyethylene[1-3] and the subsequent discovery that similar catalysts were effective in the polymerization of α-olefins and dienes to stereoregular polymers[4] were followed by a virtual flood of reports of effective catalysts and polymerizable monomers. The application of hindsight placed earlier reports in the framework of the newer discoveries, and foresight rapidly expanded their scope and began to define their limitations.[5]

Although early attempts to define the conditions necessary for stereocontrolled polymerization indicated extreme confusion, subsequent experimental data have thrown light on the questions of mechanism, that is, free radical versus ionic, and reaction conditions, that is, homogeneous versus heterogeneous.

We now see that polymerizations initiated by free radicals, carbanions, and carbonium ions are all effective under appropriate reaction conditions in initiating stereoregular polymerization. Regardless of mechanism, the underlying principle is control of the propagation reaction by immobilizing, complexing, and orienting each individual monomer before it is introduced into the chain and chemically attached to its predecessor. The nature of the monomer is the major single factor in defining the necessary reaction conditions. Although both polar and nonpolar monomers are polymerizable to high molecular weight polymers in homogeneous systems, nonpolar monomers such as the α-olefins may require heterogeneous sites that tie down and orient the monomer units to yield stereoregular polymers. Monomers containing polar substituents are capable of undergoing stereoregular polymerization in homogeneous systems through the intervention of a transition state stabilized under favorable conditions of monomer structure, solvent nature, and temperature.

In this paper, some of the catalytic processes that have been reported to yield stereoregular polymers will be examined in order to point out the effect of reaction conditions on stereoregular polymerization.

Anionic Polymerization

Ziegler-Natta catalysts. In general, Ziegler-Natta catalysts result from the reaction of two different species of metal compounds: (1) com-

*This paper, illustrated with slides, was presented at a meeting of the Section on March 1, 1960

pounds of groups IV-VIII transition metals; and (2) compounds such as metal hydrides and alkyls capable of giving rise to hydride ions or carbanions. These catalyst components need not necessarily be supplied per se, but may be formed *in situ*. Thus titanium dichloride, titanium borohydride, and irradiated titanium tetrachloride are effective single-component catalysts for the polymerization of ethylene due to their ability to complex with the olefin.

The polymerization of ethylene to a linear polymer can be carried out in either a homogeneous or a heterogeneous system, since no stereoregulation is involved. The stereoregular polymerization of propylene and other α-olefins requires a heterogeneous catalytic system. Heterogeneity is a necessary, although not sufficient, requirement for the preparation of stereoregular polypropylene. Thus the soluble reaction product of an organoaluminum compound and a transition metal compound, chemisorbed on an amorphous substrate, polymerizes α-olefins to amorphous polymers. The same organometallic compound used with a crystalline substrate derived from a transition metal halide (for example, $TiCl_3$, $TiCl_2$, VCl_3 or $CrCl_3$) polymerizes α-olefins to crystalline polymers.

The relationship between monomer structure and the conditions necessary for stereoregular polymerization is shown in TABLE 1. Homogeneous conditions are suitable for the polymerization of ethylene and monomers containing polar substituents alpha to the ethylenic double bond. A surface is necessary for the stereoregular polymerization of α-olefins, as well as for the 1,4-polymerization of conjugated dienes. Soluble catalysts polymerize dienes to 1,2-polymers, the second double bond acting as a polar substituent.

TABLE 1

STEREOREGULAR POLYMERIZATION WITH ZIEGLER-NATTA CATALYSTS

Homogeneous:	*Heterogeneous:*
Ethylene	Ethylene
	α-Olefins
Dienes ——→ 1,2-polymers	Dienes ——→ 1,4-polymers
Vinyl chloride	
Alkyl vinyl ethers	
Vinyl esters	
Methacrylic esters	

The reaction of an organoaluminum compound and a titanium compound results in the formation of alkyl titanium compounds and bimetallic complexes. In early studies by Ludlum and his co-workers,[6] as well as by Friedlander,[7] it was concluded that an active heterogeneous catalyst

for ethylene polymerization contained titanium with a valence of two or three. On the other hand, the work of Natta[8] and Breslaw[9] and their co-workers indicated that a higher valence of titanium is present in an active soluble catalyst.

FIGURE 1 indicates the structures of the bimetallic complexes that have been isolated or proposed for Ziegler-Natta catalysts.

Although complexes I and II have been isolated from mixtures of catalyst components that are effective for the polymerization of ethylene, the complexes per se are not particularly active catalysts. Apparently, the presence of other reaction products is necessary to produce an active catalyst.

Natta[10] has proposed that an electron-deficient complex is the heart of an active catalyst. In the case of ethylene, the complex may be soluble or chemisorbed on the surface of a crystal lattice. In the case of α-olefins, the complex must be bound on a surface to yield stereoregular polymers.

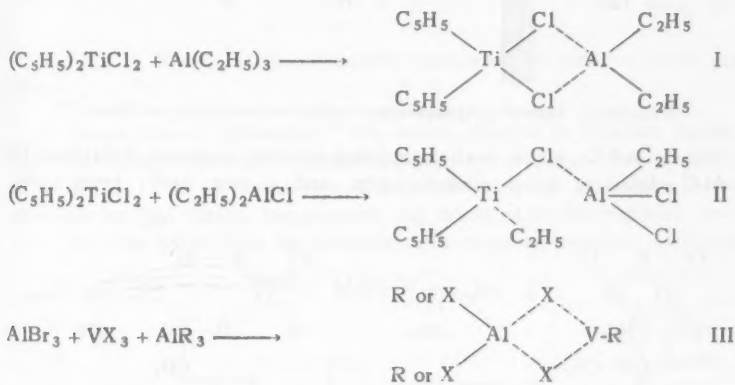

FIGURE 1. Bimetallic complexes isolated (I,II) or proposed (III) for Ziegler-Natta catalysts.

The anionic coordination mechanism proposed by Natta (FIGURE 2) involves an attraction of the π-electrons of the olefin molecule by the complex, compensating for the electron deficiency of the complex. As the monomer approaches the polar bond $M^+ \ldots {}^-C$, it becomes polarized and forms a transition state of two coordinated dipoles, followed by incorporation into the growing chain (FIGURE 3).

Patat and Sinn[11] have also proposed an electron-deficient complex mechanism (FIGURE 4). During the cleavage of the Ti-C_3 bond, the π-electrons of the olefin become associated with the 3*d* electrons of the titanium and form a new deficient Ti-C_1 bond. The Ti-C_1-C_2 bond system rotates freely around the titanium and swings into the complex.

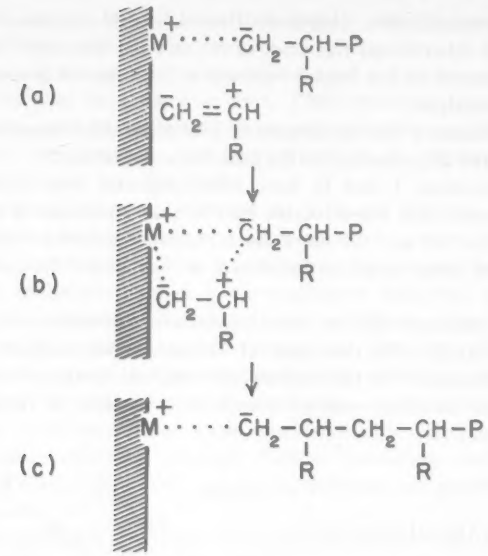

FIGURE 2. Anionic polymerization mechanism according to Natta.[10]

The C_2 and C_3 atoms, both possessing residual valences, hybridize, the Al-C_3-deficient bond disassociates, and a new Al-C_1 bond forms.

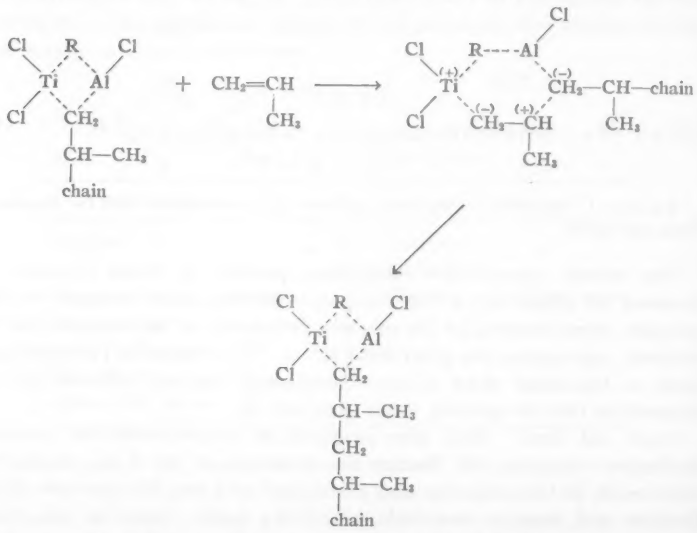

FIGURE 3. Incorporation of monomer into polymer chain.

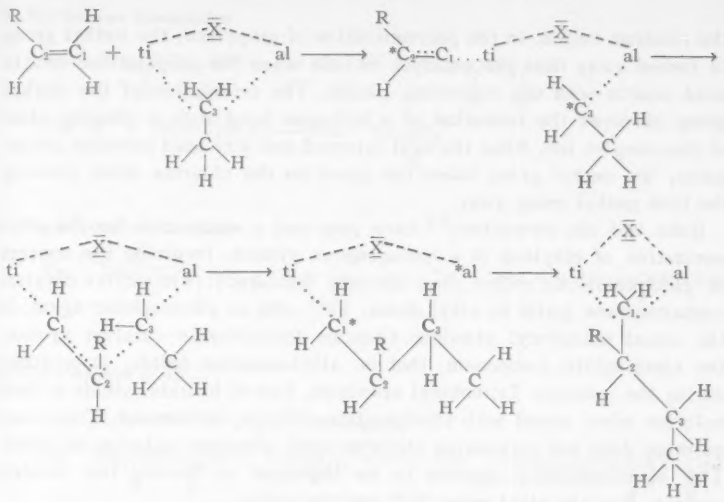

FIGURE 4. Electron-deficient complex mechanism according to Patat and Sinn.[11]

As suggested by Uelzmann,[12] the active species in titanium halide-aluminum alkyl-catalyzed polymerizations contains titanium cations (FIGURE 5). The polymerization of an olefin involves activation of the monomer on this cation, the positive end orienting to the negative complex ion. The latter pulls the olefin into the negative complex, reforming

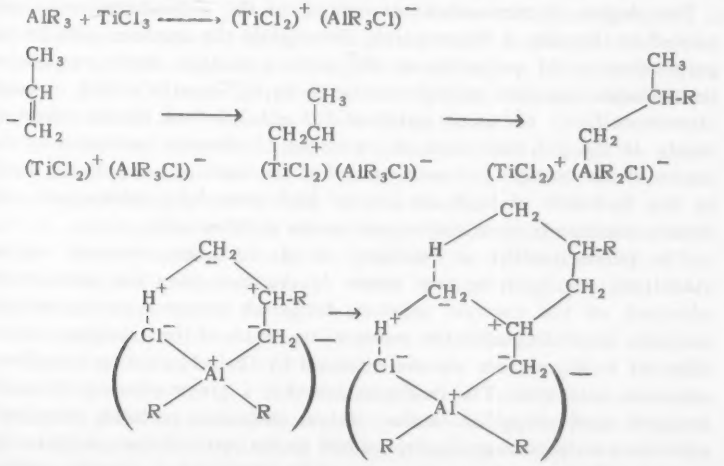

FIGURE 5. Anionic polymerization mechanism according to Uelzmann.[12]

the titanium cation. In the polymerization of propylene, the methyl group is turned away from the catalyst surface when the prepolarized double bond reacts with the activating cation. The orientation of the methyl group involves the formation of a hydrogen bond with a chlorine atom of the complex ion. When the next oriented and activated monomer propagates, its methyl group takes the place on the chlorine atom, pushing the first methyl group away.

Roha and his co-workers[13] have proposed a mechanism for the polymerization of ethylene in a homogeneous system, involving the concept of electrophilicity rather than electron deficiency. The active catalyst contains three parts: an alkyl donor, Ti^{4+}, and an electrophilic agent. In the usual triisobutyl aluminum-titanium tetrachloride catalyst system, the electrophilic component, that is, alkylaluminum halide, is produced during the reaction. Triisobutyl aluminum, free of hydride, yields a clear solution when mixed with titanium tetrachloride in benzene. This clear solution does not polymerize ethylene until aluminum chloride is added. The electrophilicity appears to be important in forming the catalyst complex from the alkyl metal Ti^{4+} and the olefin.

Beyond the concept of catalyst complexes lies the experimental observation that an active catalyst results from a component composition in which the Al/Ti molar ratio is greater than the unity required stoichiometrically for complex formation. Apparently, excess aluminum alkyl and monomer are adsorbed on the active sites, polymerization occurring at a maximum rate when both are adsorbed at a definite concentration. At low ratios not enough AlR_3 is adsorbed, while at high ratios not enough monomer is adsorbed.

The degree of stereochemical control of the polymerization is not related to the rate of the reaction. Thus while the maximum rate in the polymerization of propylene at 60° with a triethyl aluminum-titanium tetrachloride catalyst system occurs at an Al/Ti ratio of 2.0, greater stereospecificity occurs at ratios of 1.0 and 3.0.[14] A similar situation exists in the polymerization of butadiene,[15] wherein variations in the nature of the catalyst components and in the ratio of components result in the formation of high *cis*-1,4- or high *trans*-1,4-polybutadiene, although maximum polymerization rates occur at other ratios.

The polymerization of butadiene or of any other monomer can be visualized as involving two steps. In the first step the monomer is adsorbed on the catalyst sites or forms an active monomer-catalyst complex. Depending upon the structure or nature of the catalyst centers, different configurations can be assumed by the adsorbed or complexed monomer molecules. The configuration that a given monomer molecule assumes upon adsorption on the catalyst surface or on being complexed with the catalyst is apparently related to the ratio of the catalyst components. The second step, namely, the addition of a monomer unit to the polymer chain, involves a "picking up" of the monomer in whatever

(a) *Spontaneous dissociation*

$$Cat^+ {}^-CH_2\underset{R}{C}HCH_2\underset{R}{C}H\text{-}P \longrightarrow Cat^+H^- + CH_2{=}\underset{R}{C}CH_2\underset{R}{C}H\text{-}P$$

$$Cat^+H^- + CH_2{=}CHR \longrightarrow Cat^+ {}^-CH_2\underset{R}{C}H_2$$

(b) *Chain transfer to monomer*

$$Cat^+ {}^-CH_2\underset{R}{C}HCH_2\underset{R}{C}H\text{-}P + CH_2{=}\underset{R}{C}H \longrightarrow Cat^+ {}^-CH_2\underset{R}{C}H + CH_2{=}\underset{R}{\overset{R}{C}}CH_2CH\text{-}P$$

(c) *Chain transfer to* AlR_3

$$Al_2(C_2H_5)_6 \rightleftharpoons Al(C_2H_5)_2^+ + Al(C_2H_5)_4^-$$

$$Cat^+ {}^-CH_2\underset{R}{C}HCH_2\underset{R}{C}H\text{-}P + Al(C_2H_5)_2^+ \longrightarrow Cat^+ + (C_2H_5)_2AlCH_2\underset{R}{C}HCH_2\underset{R}{C}H\text{-}P$$

$$Cat^+ + Al(C_2H_5)_4^- \longrightarrow Cat^+ {}^-CH_2CH_3 + Al(C_2H_5)_3$$

FIGURE 6. Chain transfer and termination processes in anionic mechanism.

configuration it is so adsorbed or complexed. Consequently, depending upon the configuration that the monomer presents to the growing polymer chain, a *cis* or *trans* addition or an isotactic or syndiotactic placement occurs.

An interesting question arises when one considers whether a monomer unit that approaches an active site with the wrong configuration is rejected or inverted. An insight into this problem is given by the recent report that, with ethyl and *n*-propyl propenyl ethers, the *cis* and *trans* isomers yield the same polymer, indicating that a common intermediate is formed as the monomer enters the polymer chain.[16]

Thus far we have discussed the initiation and propagation steps. FIGURE 6 indicates several chain transfer and termination reactions that have been proposed in the anionic mechanism. The fact that an active center remains after these steps indicates the true catalytic nature of the coordinated anionic process, as differentiated from the radical initiated polymerizations, which are not truly catalytic, since the initiator is consumed during the process.

The polymerization of polar monomers with Ziegler-Natta catalysts involves the use of solvents that influence the complexing of the monomer. Vinyl ethers, vinyl chloride, and methyl methacrylate are polymerized to crystallizable polymers by means of Ziegler-Natta catalysts in reaction mixtures containing "complexing" agents such as ethers, esters, amines, and ketones. The polar solvents apparently participate in the formation of a complex that results in the most favorable geometric

arrangement of the catalyst and the monomer for stereoregular polymerization. The reaction medium need not be heterogeneous as long as the transition state is of sufficient stability to control the entry of the monomer into the polymer chain.

Lithium-Based Catalysts

The reaction conditions, particularly the nature of the solvents, are major factors in the polymerization of isoprene to *cis*-1,4-polyisoprene with lithium and lithium alkyl catalysts. A stereoregular polymerization occurs when the polymerization is carried out in the absence of oxygen-containing solvents.

Early work suggested that a heterogeneous system was necessary to obtain stereocontrolled polymerization with lithium-based catalysts. This was based on the observation that polymerizations in heptane that gave heterogeneous systems were stereoregular, while the homogeneous systems obtained with tetrahydrofuran or other ethers gave little or no *cis*-1,4-polyisoprene.

At the present time it is considered that the surface is unnecessary, and that the stereoregular polymerization proceeds through a homogeneous catalytic mechanism that depends on the electronic structure of the lithium atom.[17] The initiation step in lithium or organolithium-catalyzed reactions is the formation of a common intermediate (FIGURE 7). The stereoregularity of the polymerization results from the C-Li bond forming a coordination complex with the monomer in the *cis* configuration (FIGURE 8). The *cis* coordination complex rearranges to an activated complex that can be represented as a six-membered ring. Monomer addition involves the reaction of a *cis* monomer molecule containing an unpaired electron on each of the terminal carbon atoms with

Initiation

$$Li^+ - Li^- + CH_2{=}\overset{CH_3}{\overset{|}{C}}{-}CH{=}CH_2 \longrightarrow LiCH_2{-}\overset{CH_3}{\overset{|}{C}}{=}CHCH_2Li$$

$$R^-Li^+ + CH_2{=}\overset{CH_3}{\overset{|}{C}}{-}CH{=}CH_2 \longrightarrow RCH_2{-}\overset{CH_3}{\overset{|}{C}}{=}CHCH_2Li$$

Propagation

$$R[CH_2C(CH_3){=}CHCH_2]_n\,Li + H_2C{=}C(CH_3)CH{=}CH_2 \longrightarrow R[CH_2C(CH_3){=}CHCH_2]_{n+1}\,Li$$

FIGURE 7. Initiation and propagation in isoprene polymerization with lithium-based catalysts.

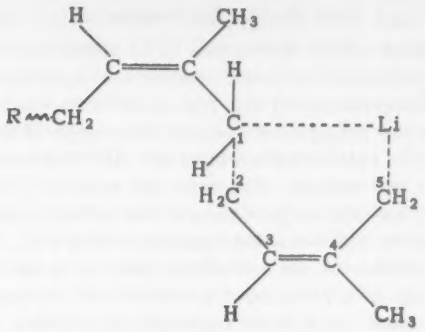

FIGURE 8. Complex formation in lithium-catalyzed isoprene polymerization.

a polarized C-Li bond. As C_2 approaches C_1, the C_1-Li bond is stretched. As C_5 approaches the lithium atom, the degree of orbital overlap becomes greater than for the stretched C_1-Li bond, the latter breaks, and the covalent C_1-C_2 bond forms.

This mechanism essentially involves the addition of a diradical to a polarized, although covalent, C-Li bond. The polar C-Li bond is dissociated by ether or other solvating agent to an ion pair. The greater the ionic character of the C-metal bond, the less likely stereoregulation occurs. Thus organosodium compounds, having a greater degree of ionic character than organolithium compounds, do not produce stereoregular polyisoprene. Ether complexes with the C-Li bond to yield ionic character equivalent to that of the C-Na bond and thus interferes with stereoregulation.

Cationic Polymerization

The polymerization of vinyl isobutyl ether to an isotactic polymer by means of boron trifluoride etherate at low temperatures was initially achieved in a "proliferous" or "polyphase" system, that is, the catalyst was present as a separate liquid phase, and the polymer slowly grew as a solid phase around the catalyst.[18] Schildknecht[19] suggested that the orientation of monomer units resulted from limited diffusion or a long-lived transition state.

Okamura and his associates[20,21] have reported that isotactic polyvinyl isobutyl ether may be prepared by cationic polymerization in a homogeneous system and have proposed[22] an interaction between the charged carbon atom of a growing polymer ion with the counterion derived from the catalyst. A repulsive interaction is proposed between the substituent of the attacking monomer and that of the polymer. The magnitude of polarization of the growing polymer ion is influenced by the nature of the counterion, by the polarity of the solvent, and even by the concentration of monomer, since the latter can solvate the ion pair.

Free Radical Polymerization

Some of the same factors that appear to be significant in stereoregular polymerization propagated by ionic species are important in free radical propagation. The character of the transition state that determines the stereocontrol of the propagation reaction is a result of the conformation into which the free radical carbon atom and its substituent are solvated by the monomer and solvent. The size and polarity of the substituent on the monomer, as well as the nature of the solvent, influence the preferred conformation of the solvated growing chain end. A monomer unit can be accommodated in the transition state by polar coordination or hydrogen bonding in a preferred orientation with respect to the chain end and hence result in a stereoregulated introduction into the chain. The effect of monomer structure on the free-radical stereoregular polymerization has been reported for the case of vinyl acetate and vinyl haloacetates.[23]

The temperature of the polymerization is a significant factor in homogeneous-phase free-radical reactions. The various transition states in which a monomer can participate are characterized by differing free energies of activation. The state with the smallest energy of activation under a given set of conditions defined by the temperature, catalyst, monomer, and solvent will be preferentially formed and will dictate the steric character of the propagation reaction. The stereoregulating influence of low temperatures has been shown in the free-radical polymerization of methyl methacrylate[24] and vinyl chloride[25] to polymers with increased syndiotacticity.

Helical Polymerization

As indicated, the chemical nature of the reaction medium or solvent plays an important role in providing a suitable environment for the formation of a preferred transition state leading to a stereocontrolled propagation step. Szwarc[26] has suggested that a reaction medium that is a poor solvent for the polymer may result in a stereoregular monomer addition to the growing chain, irrespective of the radical or ionic nature of the active chain end. If a few monomer units are linked together in a stereoregular sequence and precipitate in the form of a helix, the addition of further monomer units may be stereoregular if the rate of placement preserving the symmetry of the helix is much faster than the rate of any other placement.

The preparation of crystallizable polystyrene by the use of a triphenylmethylpotassium catalyst in hexane, in contrast to the preparation of noncrystallizable polymer in benzene,[27] has been explained[26] on the basis of the addition of monomer to the random coil shape assumed by the polymer in benzene and the stereoregular helix probably assumed in the poorer solvent.

Crystallizable poly(methyl methacrylate) has been prepared with Grignard reagent catalysts.[28,29] The nature of the reaction medium, the reaction temperature, and the nature of the Grignard reagent influence the structure of the polymer. It has also been reported[29] that the order of addition determines the polymeric structure. Syndiotactic poly(methyl methacrylate) is reportedly formed by the addition of a solution of a Grignard reagent to the monomer at room temperature, while isotactic polymer results from the addition of the monomer to a solution or suspension of the Grignard reagent at room temperature. Helical stereoregular polymerization may be responsible for this effect. Polymerization under the first set of conditions may result initially in the formation of a syndiotactic polymer, analogous to the case of low-temperature free-radical-catalyzed polymerization. Helical crystallization and phase separation may be followed by helical polymerization. The reverse order of addition may result initially in isotactic placements, followed by helical crystallization and monomer addition.

It is apparent that stereoregular polymerization results not only from the application of a particular type of catalytic species, either radical or ionic, but from the existence of a suitable environment. The appropriate geometric arrangement of monomer, solvent, and polymer can determine whether an atactic or stereoregular polymerization will occur; it also influences the particular conformation formed in the stereocontrolled propagation.

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DIVISION OF INSTRUMENTATION

OPERATIONAL CONTROL AND INSTRUMENTATION IN THE SUGAR INDUSTRY TODAY*

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Sugar from cane and beet is produced today in most countries of the world. In the tropics and subtropics sugar cane is the chief source of sugar; in the northern and southern parts of the world, usually above and below 30 to 32° latitude north or south, sugar beets constitute the primary source. The tendency is that the processing of these two raw materials is done more and more in factories using the advantages of modern engineering and technology.

The approximate world production of sugar in metric tons per annum is shown in TABLE 1.

The manufacture of a crude-sugar product from cane in the form of a concentrated juice called noncentrifugal sugar still exists to a great extent in India and in different Latin American and African countries. The total and relative quantity of this noncentrifugal sugar which, according to the country of production has local names such as gur, gula mangkok, and panela, is on the decrease, and the production of crystallized centrifugal sugars either in the form of raw sugar to be refined in refineries as a product of approximately 96° pol average or as a direct-consumption sugar is increasing. The manufacture of beet sugar is done today in almost all countries to produce a direct-consumption sugar: white granulated.

Another tendency is that the smaller units, with capacities less than 1000 tons of beet or cane, are disappearing, and the capacity of the factories as an average is on the increase. In a number of countries the average capacity of factories is approximately 3000 tons of cane or beet per day, as in Cuba, the United States, Hawaii, and Australia; in some countries a considerable number of small factories still exist, as in Brazil and India, where an average capacity of 1000 to 1200 tons of cane per 24 hours is more or less standard.

Sugar as a commodity is affected in its cost price by the wage scales of the countries of production, which vary considerably. The highest wages are paid today in the United States and Australia, where the wages for factory workers are a minimum of $1.50 per hour, whereas in such countries as India, Indonesia, and some parts of Africa, including the Portuguese colonies, the wage scale is less than one tenth of what it is

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The Section of Geological Sciences held a meeting on March 7, 1960, at which Ralph J. Holmes of the Department of Geology, Columbia University, New York, N.Y., presented a paper entitled "Geology and Mineral Deposits of Iron." This article will appear in a later edition of the *Transactions*.

TABLE 1

	Metric tons	Average capacity of sugar factories or refineries in metric tons of sugar		Number of operating sugar factories or refineries*
		per day	per year	
World production all sugars	50,000,000			
Produced as concentrated juice without modern processes or refining, noncentrifugal sugar	7,000,000			
Centrifugal sugars:				
Beet sugar production	16,000,000	250	30,000	500
Cane sugar production	27,000,000	200	25,000	1200
Cane sugar produced as raw and refined in independent refineries	18,000,000	400	125,000	140†
Cane sugar produced as direct consumption sugar	9,000,000			

*Including only factories with a daily capacity over 50 tons of sugar per 24 hours.

†The United States mainland has 20 refineries with an annual capacity of 7 million tons of sugar. The capital investment in these refineries in factory buildings and machinery is ± $200 million or, per ton of sugar refined per annum, ± $30 investment.

in the United States. This results in different levels of cost price. The cost price of sugar in different countries is shown in TABLE 2.

TABLE 2

PRICES OF SUGAR

	Per metric ton	
	raw	refined
Lowest: Mexico, Peru, Dominican Republic, Brazil, Taiwan	$ 60	$ 90
Medium: India, British West Indies, Natal	90	120
Highest: United States mainland and Hawaii, Canada, Western Europe	115	150

The cost price of sugar consists of the price of the raw material (sugar cane or sugar beets) and the manufacturing costs. The price of the raw material represents 50 to 65 per cent of the raw sugar price. The processing costs are divided among labor costs, manufacturing agents, technical supervision and management, administration and control, normal maintenance for replacement and spare parts, and costs for fuel and

power. In these cost-price data are not included interest on invested capital, or reservation for renewals and modernization.

The differences in labor wages affect the manpower use in the different areas of production. The technology, the capacity of the factory, and the degree of mechanization and automation show substantial differences. Some of the main data as to labor requirements are shown in TABLE 3.

TABLE 3

LABOR REQUIREMENTS IN MAN HOURS PER METRIC TON OF SUGAR*

	Highest	*Lowest*
Raw cane sugar	50	4
Refined cane sugar from cane	50	5
Refining raw sugar to granulated	5	0.5
Beet sugar (white granulated)	80	5

* Labor is calculated from delivered cane and beets at the factory to the refined or raw sugar stored and piled in the sugar warehouses, including precessing, steam and power generation, normal maintenance and supervision, including all skilled and unskilled labor, overseers, and mechanics.

Low labor requirements prevail in a number of plants in Australia (cane), the United States (beet and refining), the United Kingdom (refining and beet), and Germany (in new beet factories).

High labor requirements exist in India (cane), Indonesia (cane), Egypt (cane and refining), Morocco (refining), Eastern Europe (beet), Poland (beet), and Czechoslovakia (beet).

Present knowledge and experience make mechanization and automation technically possible in large parts of the world, but the decision to switch from manual handling and personal supervision to mechanization and automation is primarily a matter of economy. It is the cost factor that determines the replacement of human labor and human attention by machinery and automatic equipment. There are some rules for the replacement of manual handling by mechanical and automatic equipment. These rules, however, differ from country to country and from sugar company to sugar company.

Usually it is accepted that the saving in labor costs, to be calculated over a 3- to 5-year period, must be at least equivalent to, or preferably more than, the capital investment plus interest, plus the maintenance of the mechanical and automatic equipment, before a sugar company will decide to introduce mechanization and automation.

In a country such as the United States, the replacement of 1 laborer by mechanical equipment, for a beet-sugar factory operating 150 days, means that the capital investment of the installed equipment must be less per annum than $150 \times 3 \times 8 \times \$1.50 = \$6000$. In a country such as India the same system of calculation shows that the capital investment

for mechanization to replace one laborer should be not more than $600 per annum.

This illustration shows that what is a recommendable practice in countries with a high wage standard is unacceptable from a strictly economic point of view in a country with a low wage standard.

There is no doubt that mechanization and automation have found their well-deserved places in the modern sugar industry, and it is a matter of time and economic developments in different countries, since the wage level of industrial labor has a tendency to increase over the whole world, in that mechanization and automation will become normal and essential parts of our modern system of processing.

To give a picture of the present situation of sugar production and the developments to be expected in the future, the following consumption figures of sugar and the part sugar plays today in the human diet are presented in TABLE 4. In the United States and Western Europe sugar represents more than 15 per cent of the daily calory intake.

TABLE 4

	Sugar consumption per capita			
	Per year (kg.)	*Per day (gm.)*	*In cal.* (per day)*	*In % of daily cal. in food†*
Highest: Western Europe, U.S.A., Australia	45 to 50	130 to 145	500 to 600	15 to 20
Medium: The Soviet Union, India, Japan	20 to 35	60 to 100	250 to 400	10 to 15
Low: Indonesia, China	10	30	125	5 to 8
Lowest: Central Africa, Tibet, West Central China	<3	<10	<40	<3
Average for the entire world	16	45	<200	8 to 10

* The caloric value of sugar is taken at 4.2 cal./gm.

† The daily calory intake in food of the average individual (man, woman, child, old and young) is taken at 3000 cal./24 hours. This value is too high for the majority of the world population; for this group in Asia, Africa, and South America it is closer to 2000 cal./24 hours.

In describing instrumentation in the sugar industry, this review will be limited to control of the operational conditions in the processing of the raw and intermediary materials and the finishing of the commercial products. The measuring of these conditions is primarily a determination of physical characteristics: weights, volumes, flow rates, pressures, temperatures and densities; and some physical chemical analyses, applying physical principles, such as the determination of *p*H, color, turbidity, and conductivity.

In the processing of sugar the following elements are important: (1) the concentration of the solution to be subjected to processing, a determination almost always based on measuring the specific gravity, occasionally the refractive index or the boiling point elevation; (2) the temperature of products subjected to processing; (3) the pressure of steam used for heating or evaporation, which in factories is practically always saturated steam of low pressure; (4) the vacua in crystallization and concentration; and (5) the *p*H in purification.

In describing the traditional system of processing sugar juice or sugar liquor, we use as an example one of the important operations: heating. The laborer in charge of the heating station must operate and adjust the steam valves; he must control the temperature of the juices or liquors to be heated, and his activities are limited to closing and opening valves according to instructions as to the temperature to be maintained.

This part of the instrumentation is simple. The only instrument needed by the operator is a reliable thermometer with a visible and readable scale, eventually equipped with special marks indicating the maximum and minimum temperatures to which the sugar products must be heated. Management should expect the selected laborer to be careful in his readings and be always attentive.

This operation has been studied with recording instruments primarily with the aim of checking the performance of the operators. This is one of the technological investigations done in several modern sugar mills in Java, where labor costs were low and where it was difficult to present convincing arguments that automatic temperature control is more efficient and for this reason a recommendable change to achieve better results.

The first thing to be observed, and that needs no illustration in the form of graphs, is that when we rely on an operator to adjust the openings of a steam valve to maintain a uniform temperature of the products to be processed, a range of temperatures is covered, and deviations from the prescribed temperature are more normal than exceptional.

The accurate heating and temperature regulation of juices and liquors is important for some of the processes as, for example, the carbonation process, which consists of adding to the cane juice a large amount of hydrated lime, which is precipitated by introduced CO_2, and where the temperature must be maintained as closely as possible in cane sugar mills at 55° C. Higher temperatures cause decomposition of reducing sugars, an increase in the amount of soluble lime salts, and an increase in the color of the purified juices. In this case it can be demonstrated that, for mills operating with an annual sugar production of only 20,000 tons, automatic temperature control is an investment that is paying in one crop.

A well-known problem is to have a usable expression for the fluctuations of such recorded physical data as temperatures and pressures.

Everyone who has analyzed recordings knows that nervous jumping graphs are difficult to interpret. I have been using for the interpolation of physical operational conditions the recorded graphs, taking the readings from the graph at 3-minute intervals and measuring the recordings in this way for a period of 1 shift, or 160 data. The frequency or distribution over small temperature ranges of the collected data is noted and with these data a distribution curve is made on probability paper. In this way we have the average, and it is a matter of arbitrary decision whether we take the deviations corresponding for one sixth or one fourth of the readings above and below the read temperature on the graph. This gives a simple expression for the fluctuations; for example,

$$\text{temperature} = \text{average} \pm \frac{\text{1/6 of the observation over } T_+}{\text{1/6 of the observation under } T_-}$$

$$= 55.3^\circ \frac{+ 58.8^\circ}{- 52.9^\circ}$$

$$= 55.3^\circ \frac{+ 3.5^\circ}{- 2.4^\circ}$$

At the same time this gives us a control on the reliability of the operators or of the automatic equipment.

By the use of graphic presentation of the recorded data on probability paper progress can be made in the endeavor to have more uniform operational conditions by calculating the deviation ratio, which is by definition:

$$\frac{\text{Deviation after the introduction of any system to improve regularity}}{\text{Deviation before the introduction of such a change}}$$

This change can be: replacement of the operator by a more careful man; reconstruction of the equipment; and automatic adjustment versus manual adjustment of operational conditions.

The deviation to be used must be determined arbitrarily. For temperatures it may be the difference in recorded temperature with one fourth or one sixth of the recorded data below and over the determined temperatures. As an example, we found that with manual temperature regulation the temperature fluctuations occurred during four sixths of the time:

$$55.3^\circ \frac{+ 3.5^\circ \text{ C.}}{- 2.4^\circ \text{ C.}} \qquad \text{Deviation } 3.5 + 2.4 = 5.9^\circ \text{ C.}$$

After the introduction of automatic control the fluctuations were:

$$55.0^\circ \frac{+ 1.0^\circ \text{ C.}}{- 0.8^\circ \text{ C.}} \qquad \text{Deviation} = 1.8^\circ \text{ C.}$$

The deviation ratio between manual and automatic temperature control was:

$$\frac{1.8}{5.9} = 0.30$$

The sugar technologist must decide which fluctuations are acceptable from an operational point of view. A compromise must be found between perfection and technically and economically acceptable standards. No one in the sugar industry will ask for a temperature control with an accuracy of $\pm 0.1^{\circ}$ C., but no one can be satisfied with a heating in the phosphatation process with fluctuations of $\pm 5^{\circ}$ C. The practical standard is somewhere in between, depending on the capacity of the refinery and the effect of deviations on over-all performance and efficiency.

With average workers it is found that there are great differences as to the carefulness and reliability in operating such a simple piece of equipment as a valve to maintain a prescribed condition. It is also necessary, when these measurements have been made for manual operation, that the recording be repeated when an automatic temperature control has been installed. It is a fact that almost no automatic type of equipment gives exactly prescribed operational conditions all the time. Too many variables are involved in the processing in a sugar factory; the rate of grinding or the amount of juice or liquor treated per unit of time varies, the starting temperatures of the materials can vary, and the heating medium – the vapor – does not have a constant pressure and temperature, but fluctuates.

To find automatic equipment that makes the necessary corrections immediately when one of these variable conditions changes is almost impossible. However, one thing is certain: a well-constructed automatic temperature controller adjusts better than human operators do.

One of two phases in the field of automation is normally given attention by manufacturers: that the working conditions be analyzed before a piece of equipment is installed. The second phase, just as important, is that after any piece of equipment is installed its efficiency and performance must be checked.

It is no exaggeration to state that of the automatic control equipment installed for the heating of such ingredients as juices, liquors, syrups, and molasses, more than 50 per cent does not function satisfactorily. This is partly because sugar factories do not have reliable recording control instruments. These are instruments kept primarily for the purpose of verifying the operational conditions. It is the duty of the technologist assigned to this specific function to measure the operational conditions exactly and periodically with a special set of recording instruments of great accuracy and to keep them in first-class working condition.

In a sugar factory a number of determinations can be extremely helpful in arriving at improved results through a better understanding of what

actually is happening in the different steps of processing. I refer to some applications that have been unsolved problems in the sugar industry, but that can be answered satisfactorily only when we have a fully automatic chemical control system. I cite the problem of the quality of cane assessed from an agricultural point of view, and also the problem of introducing certain types of nonsugars in the manufacturing process. The maturing of cane is characterized by a decrease of the reducing sugars in the cell content of the cane, combined with an increase in the sucrose content. It is now customary for most factories to make an analysis of the cane juice to evaluate the quality or yield of the cane delivered by the farmers or from the plantation fields. We have at present excellent methods for the continuous recording of reducing sugars, for example, by the AutoAnalyzer. It would be of great advantage to install recording analyzers in the factories to determine the quality of all the cane delivered to the mill. By properly timing the discharge of cane to the mill carrier and by synchronizing it with a certain time lag according to existing operational conditions for the recorded reducing sugar content of the mill juices, a fundamental knowledge can be obtained as to the behavior of different varieties and the effects of field conditions and fertilizer practices on the maturing of cane.

The question may be asked: Why should a mill make such a study? The answer is: First, to give guidance and information to the farmer. However, there are two parties involved, and the factory can take the attitude that it should not instruct the farmer as to how to harvest well-matured cane. When the cane is not mature, and the factory pays on yield, the farmer incurs a penalty for the deficient quality of the cane. The point is, however, that the farmer is not able to make this kind of analysis. It is the cooperation of factory and farmer that can provide the understanding necessary to real progress.

Another point in the same category of problems is the analysis of phosphates in cane juices. There are areas and specific years that the phosphate in juices is low; this juice component is essential for good clarification. When an analysis is made of a juice occasionally and the phosphate content is found to be low, the factory management begins adding phosphates or other chemicals to the juice to compensate for the presumed shortage. However, it is certain that in many cases an excess of phosphate is used when there is no need for it.

A recording of the phosphate content of mill juices determines immediately whether it is necessary to use additives. At the same time it would give valuable information to the farmer as to which cane fields are rich in available phosphate and which are low. Where the cane is high in phosphate any use of phosphate fertilizer is a luxury application and where it is low it is worthwhile to make experiments on the effect of phosphate fertilizer in improving the productivity.

Automatic control equipment now has found its well-deserved place

in sugar technology. The application of automatic equipment for the control of operational conditions is not an exclusive matter for manufacturers of this equipment; such equipment must be investigated carefully by the sugar technologist wherever this equipment is installed.

From the experience collected it is evident that automatic equipment is in most cases far superior to manual adjustment. There is every reason to believe that in the next decade the control of temperatures, concentrations, pressures, alkalinities, and the concentration of reagents will be done more and more automatically, not only for technological reasons but also for reasons of strict economy. The replacement of the human element, with its attendant monotony of operation, is a development of the present era and must be accepted as a substantial contribution to progress, both technically and economically.

SECTION OF BIOLOGICAL AND MEDICAL SCIENCES

THE DANGER OF SIMPLIFIED ECOSYSTEMS*

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One of the characteristics of what is called cyclicism in populations of animals but is more accurately a constant pattern through time of fluctuation in numbers is that the phenomenon is more marked in the subpolar regions and declines to negligible proportions equatorially. Variation on this general statement may be observed in deserts where cyclicism is apparent although the deserts are in the tropics. The criterion, in fact, is not latitude but the degree of simplicity or complexity of the biological community. The animal populations of simple communities tend to fluctuate over a period of years, the 3- to 4-year cycle being a common one for small rodents such as voles and lemmings, and 10 years for somewhat larger ones such as the muskrat. Dependent predatory animals vary in somewhat longer cycles. No one has demonstrated cyclicism of rodents in the tropical rain forest of British Guiana, which is one of the most complex communities of plants and animals on earth (Paul Richards remarks, for example, that there are 3,600 species of woody plants with a trunk diameter of 20 cm. or more).

Nature is not simple, despite the discipline of form and function: nature is as complex as the conditions of environment allow, for animate nature is concerned with circulation of energy as a consequence of conversion of matter. A simple biological community (one of relatively few species) is an expression of limitation of environment. The observable phenomenon of ecological succession in biological communities, succession from extremely simple pioneer or colonizing communities to such ecological *continua* as the environment will sustain, is the basic process of increasing such complexity as time and environmental conditions will allow. Complexity of a biological community means integrated increase in numbers of species. Each member of the community has found a niche in which it can persist, a function it can perform in the conversion cycle of matter.

A continental tropical rain forest represents the oldest and most complex life form known. The degree of integration and delicacy of niche structure is such that conversion of matter is very rapid and the visible expression is the immense biomass of plants and animals. Some pragmatic assessors of natural resources proclaim the rain forest to be very rich as an area that might yield animate resources to mankind. Their great mistake is in interpreting a biological phenomenon as a potential environ-

*This paper was the first of three papers presented at a meeting of the Section on March 14, 1960.

ment for a simplified biota of their own choosing. The ecologist sees a rain forest with an increasing awe as he better comprehends that its wealth is in its complexity, which makes possible the steady, rapid conversion cycle. Above and below ground level the process continues with an incredible efficiency, dissipating so little of the energy in circulation, but holding great masses of matter as in a reservoir, in the durable bulk of trees. If, failing to comprehend that the wealth of the tropical rain forest is in the complexity of its biological community, the exploiter clears the forest to grow crops of food or fiber, he tends to find he is left with nothing. The sun and warmth oxidize the organic matter of the soil, and the water washes away what is left.

This is the extreme case, the shattering descent from the beauty of ecological repose to the stark horror of an eroded landscape, a descent so rapid that certain intermediate phenomena are scarcely observable. However, there are many other environments in both tropical and temperate zones where the consequences of disturbance of biological communities by simplification present serious problems of management.

Much of the land of the central and east African plateau is in this category. The fauna of Africa is unique in its variety and in the time through which it has developed undisturbed: no series of glaciations or vast upheavals or land sinkings have severed it from the Pleistocene Period. The spectacle of an array of African animals in wild African country is one of the finest on earth and few civilized people have failed to be moved by its significance. The fact of the variety of the ungulate fauna of Africa means that land carrying this fauna unimpaired is being very fully utilized. To cut down the variety of grazing and browsing species from twenty to two domesticated species, cattle and sheep, is to limit the range of utilization, and throw the grazing complex out of balance.

The land-use ecologist does not question the increased fruitfulness that can result from bringing good land under a system of wise farming. What he does question is the rightness of disturbing the plant and animal communities of lands marginal and submarginal to agriculture and pastoralism, lands that rapidly deteriorate under such usage. If a country is not adapted to farming, the ecologist would suggest that the human population should adapt its husbandry to harvesting that which the country naturally offers.

Recent agronomic research shows that land grazed by cattle and sheep is the better maintained if some of the wild hoofed animals also use it. Harvesting of the wild hoofed animals as a source of protein for a protein-starved continent is feasible and practical and, in the view of many, controlled harvesting would be the surest means of conserving the herds in large parts of Africa.

AREA-RESOURCE DEVELOPMENT*

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Citizens of the United States have become convinced of the importance and indispensability of natural resources. The serious student of conservation can cite a number of case histories to illustrate good performance; unfortunately, he can usually cite an equally large number to illustrate poor performance. Advances in the field of forest management have been gratifying; the handling of space allocation for best use has been less satisfactory.

Much success in the conservation field has come about as a result of the institutional arrangements established at the federal level. Generally, the idea has been accepted that management and allocation of resources require federal planning, for otherwise a "balance wheel" would be lacking. Private entrepreneurs cannot be expected to develop resources independently in such a way as to maximize long-range benefits to the nation. This idea has been institutionalized through the establishment at the federal level of a number of resource-oriented agencies and a considerable body of resource legislation.[1-2]

The backlog of federal experience should be duplicated at the state and local levels. There are sound reasons for this.[3] The nation, now mature, faces major policy problems in such fields as space exploration, development of nuclear energy, international trade, and aid to underdeveloped countries. The federal government should not be expected to continue expanding its resource agencies, particularly those concerned with internal resource problems and, at the same time, to establish new agencies to handle the many new policy areas that are arising. There is ample evidence that many internal resource problems can be handled by state and local governments once the necessary institutions are established. Many states are already doing excellent work in the conservation field. Very little is being accomplished, however, by metropolitan communities. It is this problem – inadequate resource planning in urban areas – that I shall deal with in this paper.

Resource Problems and Urbanization

Some of the nation's most important internal resource problems are being created by the rapid trend toward urbanization.[4] The most dramatic character of this urbanizing process is concentration and congestion of people within relatively small areas with limited resources. Resource problems created by urbanization are not different in kind from those

*This paper, illustrated with slides, was the second of three papers presented at a meeting of the Section on March 14, 1960.

encountered in the past. They differ only in the nature of the process that is creating them.

In few instances have urban community leaders shown themselves capable of solving resource problems. Greatly accelerated population increase has frustrated many an attempt to guide urban growth. Those who have worked in local government are aware of one of the major difficulties. Day-to-day handling of social welfare, education, and related problems arising from human needs leaves little time for proper management of the urban environment.

It is disheartening to report that most resource problems in urban areas are being solved the easy way: by tending to consider resources inexhaustible. The process follows this course: site resources (those within the confines of urban areas) are developed in an uncoordinated and independent manner by private citizens, government agencies, and industries that pay little attention to inherent physical and biological characteristics. No one attempts to assess the capacities of the resource base in the community; urban communities do not have unified policies for the development of resources other than those regulated by the market place. Most communities are unaware of what happens in neighboring areas with respect to resource development. As a result, site resources are depleted quickly and depreciated wastefully. Then community leaders, groups of wealthy citizens, and industries look elsewhere for additional resources. This process is made convenient, of course, by the automobile, train, pipes, pumps, and other technological advances in transportation and communications.

Water Management, An Example

I shall discuss only one example of poor resource planning in urban communities, and shall generalize about water-management problems on the basis of experience with this problem gained while working on a county-planning commission in southeast Michigan.

In urban communities there are a number of water needs that must be satisfied: municipal consumption, sewage assimilation, industrial processing and cooling, power generation, recreation and, in fringe areas, truck-crop irrigation. Incorporated govemment units and private entrepreneurs, having powers to do so, usually attempt to provide themselves with facilities to satisfy most of these needs. However, for fifty years there has been much study and experimentation with techniques at the federal level for coordinating and integrating the facilities that are constructed on rivers. Integration of plans for single-purpose facilities has been recognized, on the basis of physical and economic realities, as the most desirable conservation approach to water management.[5]

A stream is a natural unit having inherent capacities and limitations that condition the uses that can be made of it. The proper management of

a stream has nothing to do with political boundaries or with the construction of facilities by independent powers. Management must be based on hydrology, meteorology, geology, and engineering. Allocation of water supplies must be determined on the basis of maximizing economic benefits and satisfying recognized albeit sometimes intangible social values.

Again and again we hear of individual communities or private entrepreneurs that deplete and depreciate stream waters within urban communities and then look elsewhere for additional supplies, sites to dump excess sewage, or pollution-free recreation areas. For some reason, the concept of joint management is not grasped. This would entail integrated development and location of facilities so as to utilize fully the capacities of urban streams, and it would mean adjusting land uses to the most economical water-management scheme.

The important point in this connection is that uncoordinated, intensive development leads very quickly – in fact, prematurely – to wasteful depreciation of urban resources. Completely oblivious of the value of assessing the capacities of site resources, most communities continue to grow and develop urban land uses that only aggravate the resource situation. The solution has been development of highly expensive facilities that reach outside the confines of the urban community. It is partly this process and its consequences that lead communities to a bankruptcy of facilities. In a recent study of facility costs in Los Angeles, Calif., it was estimated that each additional family would cost the community approximately $13,000 over the next twenty years.

The Answer: Comprehensive Planning?

Problems such as these are easily identified. It is much more difficult to solve them and to suggest the institutional arrangements that are needed. There has been considerable speculation on these matters and, of course, communities do have the backlog of experience at the federal level for guidance.

What is the answer? Comprehensive planning? Intergovernmental cooperation? Integration? Unified development policy? Are not these idealistic terms? Perhaps so, but they symbolize our best thinking regarding resource problems, and they give us objectives for further achievement.

The Answer: "Muddling Through?"

Charles Lindblom[6] has shown us how difficult it is to approach such problems in a completely rational manner. With a change in situation to fit my example, this is the story he tells.

Suppose that an administrator has been given the responsibility to recommend policy with respect to development and management of a small stream in an urbanized belt of communities. This is what he might do. He might start by trying to list all related values in order of importance,

including water supply and sewage disposal. In the case of a highly developed urban area, he would note the capacities of the stream under proper management to satisfy these values. He would also identify such noncomplementary values as recreation and sewage disposal.

In this way he could rate all possible outcomes as more or less efficient in attaining a maximum of these values. In comparing possible outcomes, he would take note of any theories having to do with water and land management that generalized about any one of his policies. Finally, he would present a plan that maximized the values. This is an operational definition of the terms comprehensive planning and integration and unified development policy.

An alternative approach – the one most commonly used in urban communities – is to begin by establishing a principal objective, that is, obtaining additional water supplies for a community. The administrator might complicate the task by adding one other goal, for example, recreation, but beyond this he would disregard most other values. He would not concern himself, for example, with the effect of his water supply policy on other water uses, on the water supply policy of neighboring communities, or on the land policies developed by another administrator in the same urban community.

Next, he would outline the relatively few policy alternatives that might occur to him. There would be little need of looking for a body of theory to carry through the operation. Instead, the administrator would rely principally on past experience, and he would arrive at his ultimate recommendation quickly and easily.

Muddling through, the expression used to describe the latter procedure, sounds more like the gambler's term than that of an administrator. However, it does have a familiar ring with respect to local government operations. When an administrator attempts to establish policy in a local community, the odds are in his favor if he can substantiate his plan with sufficient group support. Then, again, he may have providential luck. If his project happens to be flood control and, in the course of his deliberations, a devastating deluge occurs in his area, he is assured of support for whatever program he suggests.

The Challenge to Conservation

It is apparent that much better work must be done in what may be called broadly area resource development in urban communities. Today, considerable research on urban problems is being undertaken by geographers, regional economists, planners, and political scientists. Most of the concepts, principles, and theories that these groups are developing apply to urban design and to physical, economic, and social planning. There is a definite lack of orientation toward resource management.

The challenge to conservation is to refurbish resource concepts and theories so they can be applied to the urban situation (earlier, I mentioned that the urban problems are not new in kind). The purpose of such activity should be to integrate knowledge of ecological and resource management with current research on urban problems. Research is only one half the answer. Education is needed to stimulate better and more aggressive leadership at the local level. Past successes in handling resource problems at the federal level and the institutions that have been established to accomplish these successes should serve as encouraging guideposts. Urban communities need more professional talent, more funds, and more planning powers before they can see the problems through to solution.

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CULTURE PATTERNS AND RESOURCE MANAGEMENT*

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The object of this paper is to make clear the importance of social science in conserving our natural resources. To this end I shall attempt a brief analysis of: (1) the activity we call conservation; (2) the role of science in conservation; and (3) the relevant aspects of social science, concluding with a few appropriate, concrete examples.

What is Meant by Conservation

Like most words, the term conservation has undergone considerable evolution. Even now it does not carry the same connotation to all people. Many have developed concern because of their interest in a specific resource such as trees, soil, water, or wildlife. Others have approached the problem as one of economics, aesthetics, ethics, politics, or natural science. Whatever the source of interest, it tends to give rise to a heavy emotional involvement. This makes a cool appraisal all the more necessary.

Certainly all of the factors just mentioned enter into the picture. Account must be taken of those who wish to enjoy the present beauty of the landscape no less than those who wish to ensure a reasonable abundance of the necessities for future generations. Consideration must be given to the fact that different individuals see different possibilities and wish for different benefits from the same resource or group of resources. It is this, more than any innate perversity of human nature, that explains why almost every resource problem involves a conflict of interest.

It is by now quite evident that no answer can be developed for any single resource in isolation from the rest. One cannot conserve fishing without attention to water, hence to the disposal of industrial and domestic waste and the loss of soil from farms. Sound forest policy depends upon proper apportionment of land use for this and other purposes. Crops of wildlife cannot be produced on land that has been allowed to become infertile. All conservationists find themselves ultimately in the same position.

This statement appears to hold also for those whose approach is philosophical but who may start from different premises. I find in my analysis of any given landscape that the result is much the same whether I begin with a balance sheet or a visual appraisal of what may be called the "health" of the area.

Thus the complications are more apparent than real. Conservation is

* This paper was the third of three papers presented at a meeting of the Section on March 14, 1960.

not primarily an operational matter, for example, of choosing between hoarding and scrambling for substitutes. Instead, it is fundamentally a question of what the Quakers call concern. The unifying thread is a responsible attitude of men toward their environment.

The Role of Science in Conservation

It is a curious paradox of this scientific age that the strongest justification for the pursuit of science is the least regarded and used. Science is an expression of the creative impulse in man. It is also a source of great practical achievements customarily referred to as benefits. However, most important of all, it should minimize areas of uncertainty and give humanity a perspective on its relation to the rest of the natural world. In other words, science is an indispensable guide to responsible conduct with respect to environment and hence toward resources.

In practice we find science applied chiefly to speeding up the elaboration of consumers' goods from raw resources and to reducing the death rate but not the birth rate. The obvious effect is a concurrently rapid increase in population and in per capita, hence total, consumption of materials and energy. In so far as these basic items are finite in amount – at least in readily available form – this process is one of living on capital and is equivalent to treating depletion and depreciation as income rather than as liability.

Emerging from this situation is an interesting rationalization known as the necessity of an expanding economy. This holds that human welfare must depend upon more and more customers, using more and more things and discarding them more and more rapidly. Joseph Wood Krutch[1] calls attention to a recent documentation of this point of view, mentioning a pamphlet called *Consumption for Prosperity*. Of considerable interest is a new volume *Science and Resources*.[2] Here a group of distinguished individuals discuss the prospects and implications of technical advance. We are assured of an impressive abundance of wonders that will be forthcoming. However, here and there – notably in the editor's introduction – we are warned that things cannot go on at the present rate forever.

Long ago John Stuart Mill, in a chapter called "The Stationary State,"[3] made clear the necessity for some kind of dynamic equilibrium in the political system. Much more recently Joseph Spengler[4] has shown how this applies to unchecked urban expansion: after a certain optimal size is reached, each increment becomes a liability instead of an asset. The annals of biological experiment show consistently that no known organism can increase its numbers indefinitely (even if it does not increase its per capita consumption) without coming to terms with parameters in the environment. History indicates that this applies to man as well as other forms of life (see Samuel II, chapter 24).

Strangest of all, however, is lack of concern among the apostles of an expanding economy and population over the implication of certain

basic principles that they scrupulously respect in the technology upon which they base their faith. It is, I believe, sound physics to state that, when dynamic units are confined in space, any increase in numbers or energy diminishes the measure of freedom of each unit. Men, no less than molecules, are dynamic units. The livable earth, no less than a liter flask, is finite in measure. Our numbers are increasing at a rate without precedent in world history, and so is the energy at our present disposal. The universal motor car increases pressure in our system as truly as heat applied to a flask of molecules.

One cannot in conscience object to prophecies and promises based upon science. However, it is hardly scientific to ignore the caveats that are quite as substantially based.

The Social Sciences

Until recently, social science suffered from the same defect as pre-modern medicine. Both disciplines were too preoccupied with pathology, too little concerned with health and the normal. There was an important difference, however. The physician generally knew sickness when he saw it. The student of society was inclined to regard any system but his own as somehow abnormal. Thus he furnished a kind of intellectual justification for missionary and colonial effort, and for the expansion of trade at whatever cost to other social systems, their resources, and environmental adjustments. Africa, for example, was in excellent ecological balance until invaded by Europeans.

However, social science has changed. Just as geology was transformed by the assumption of uniformity, so has social science profited by adopting a fairly simple working assumption. Each group is regarded as having developed its own pattern of behavior and values, that is, its culture. Each culture has its own internal logic, is worthy of serious and respectful study on its own merits, and must be studied from within, so to speak. Proceeding on such a basis, social scientists have amply justified themselves.

For our present purpose, two important considerations emerge. One is that the intangible values of a culture are decisive in shaping the standards of group and individual behavior.[5] The other is that the relation of a population to its environment is a function of its culture pattern.[6-8] A corollary is that, to improve the relation between a culture and its resources, one must work to modify the culture pattern. This must be done in terms of the pattern itself, using the dynamics that it itself provides. Since values, or sanctions, determine behavior, the values of a culture can be modified best by means consistent with them.

Thus a group of southwestern Indians changed their destructive land-use practices through the influence of a new neighbor who was a superb rodeo rider, although appeals from competent technical personnel had

been useless. Again in our own culture, which assumes the importance of private enterprise, the corporate structure of lumber and pulp companies has brought about vast improvements in forestry. The very necessity of maintaining a permanent supply of raw material, that is, the duty of corporation management to keep it in business, has been largely responsible. It is, however, a pleasure to record evidences of concern for the public welfare accompanying this self-interest.

Fortunately our culture pattern, complex and diverse as it is, has instruments of change consciously built into it whose effectiveness is evident in soil-conservation districts, watershed and valley associations, and special organizations, national and local, too numerous to mention yet most effective in the aggregate.

Substantial as these achievements are, no one has seriously come to grips with the central dilemma in resource management in our culture. As yet we seem committed to the philosophy of unlimited expansion, and more inclined to hear the promises than the warnings of science. We are victims, not of the kind of illiteracy referred to by the Spanish word *analfabetismo*, but of a different level that can read but not discriminate. We must work unceasingly for better education, which should include science. However, any effort to concentrate on science to the exclusion of history and the arts will surely be self-defeating. Only when substantial numbers of our citizens have absorbed confidence in the order of nature and can view themselves in the perspective of human experience can we expect that responsible attitude toward our environment that I have called conservation.

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DIVISION OF SPACE RESEARCH

RADIO ASTRONOMY AND THE NEW NATIONAL OBSERVATORY*

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One need only look up at the sun by day or at the stars by night to understand why astronomy has such a long history as an observational science. Despite some early confusion with respect to the size, shape, and position of our own planet relative to the sun and stars, man recognized quite early the fundamental role of the sun as a source of light and energy. The moon and brighter planets, which sometimes could be seen by day, moved relative to the sun and stars, all of which partook of a daily motion from east to west across the sky. It was further observed that the sun, moon, and planets had cyclic motions northward and southward, and all of these observed events were found to be related to things that directly influenced our own activities – the tides, the feeding habits of birds, beasts, and marine life, the seasons and the spring flowering of the fields or the autumnal coloring of the forests. Peoples interpreted these things in a variety of ways and reacted accordingly. We should not be surprised by the frequent occurrence of sun worshipers or of astrological beliefs and explanations that prevail to this day. We should not be surprised that early peoples related groups of stars to legendary characters or things, real or imagined, that survive to this day in the familiar constellations. However, we should not let these things blind us to the fact that early scientists and engineers put astronomy to good use. We should greatly honor and respect Eratosthenes of Alexandria, who in 250 B.C. reasoned that the earth was a sphere and proceeded to determine its size from the observed difference in elevation of the sun at two stations separated a measured distance along a meridian. Other examples could be cited on the early feats of navigation or on the design and orientation or alignment of structures still standing. The invention of the telescope improved the quality of astronomical observations, but it is important to note that Newton's formulation of modern mechanics was based on a mass of observational data that preceded the telescope. In more recent times, as the quality of our observations improved with the development of better telescopes, the photographic plate, the spectrograph, and the photoelectric cell, man's understanding of the universe grew – man now realizes that our sun

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is but a star located at an inconspicuous, off-center position in our Milky Way system, which is but one of many galaxies.

Except for an occasional meteorite that plunged in a fiery manner to the surface of the earth, man's knowledge of the universe was limited to what he learned in the visual observations that have been reviewed. In 1932 this observational limitation was drastically changed, but few professional astronomers recognized it for more than a decade. Karl Jansky[1] was a young engineer working for the Bell Telephone Laboratories at Holmdel, N.J., assigned to study the radio interference of thunderstorms with the then relatively new problems of transatlantic radio communications. As Jansky analyzed his data, he discovered that there was a small diurnal variation of the interference, or static, and that the time of the daily maximum progressed slowly with the season. He determined that the maximum coincided with the passage of the Milky Way across the meridian and correctly concluded that he had obtained radio signals from celestial sources. A new branch of the ancient science of astronomy had been discovered – radio astronomy.

The light we see from the stars and the radio static Jansky recorded from the Milky Way are physically the same, except for one important parameter, namely, the wave length or frequency. The light we see or photograph has a wave length of the order of twenty millionths of an inch. Radio wave lengths in use today vary from an inch or less to a mile or more. All are electromagnetic radiations, but different means of observation or detection are required, depending on the wave length. The transparency of the atmosphere varies with the wave length of the electromagnetic radiation. The light we see obviously comes through the atmosphere. Light with wave lengths shorter than that of blue is blocked, at least at sea level; those of us who have received a severe sunburn when on a high mountain know that there is much ultraviolet and that its intensity increases the greater the portion of the atmosphere we have below us. For wave lengths only slightly greater than visual red, the atmosphere is opaque. It is also opaque for many radio wave lengths; but for a band of wave lengths from about one-half inch to ten yards, the atmosphere is transparent. This radio band is much broader than the visual band. In musical terms, the radio band is approximately eight or ten octaves wide, whereas the visual band is only about one octave.

The importance of the wave-length variation between visual and radio astronomy can be appreciated better from a few illustrative examples. We are familiar with the problems of devising an achromatic lens or photographic emulsion to perform perfectly over the octave of the visual band. The ten-octave radio band imposes challenging and difficult problems for the designers of the necessary instrumentation for radio astronomy. With a few trivial exceptions, no one has yet designed and built instruments that are suitable for the entire broad band.

The vast difference between the visual and radio wave lengths permits certain measurements to be made more easily or with greater precision for one than for the other. For example, radio techniques are generally better for the measurement of a wave length or frequency. On the other hand, visual instruments are better for measuring the angular position of a celestial source. This and the related problem of resolution will be developed a little more, because they will enter into later discussions of radio telescopes.

The ability to distinguish between two sources very close together in the sky and the precision with which a telescope may be pointed at a single object are limited in an ideal instrument by its resolution, which is measured in terms of the ratio of the wave length to the diameter of the objective lens or primary mirror. This ratio for the average human eye under normal conditions is about 1:5,000; in more usual angular terms, the eye has a resolution of 1 minute of arc, or a little less. For the 200-inch Hale telescope at Palomar Observatory, Pasadena, Calif., the ratio is almost one billion and the theoretical resolution cannot be achieved because of the twinkling effects introduced by the atmosphere. For a nominal radio wave length of about 1 foot, the aperture of a radio telescope would have to be 1 mile in order to provide no more than the resolution of the eye. Astronomers would like to have such a telescope, but it has not yet been designed or built.

We have noted already that the atmosphere absorbs electromagnetic radiations of certain wave lengths and is transparent for others. The physical reasons for this apply throughout the universe and are of tremendous importance to astronomy. The great volumes of space between the stars are vacuums by our laboratory standards, but actually contain dust and gas that in total are a significant portion of all the known matter in the universe. We are familiar with the absorption of visual light by clouds of dust and gas, and astronomers observe similar interstellar absorption effects. On the other hand, we know that some radio wave lengths can penetrate clouds of dust and gas with little absorption – television continues to function during a dust storm, radar can operate in fog, and radio wave lengths can penetrate the interstellar clouds. A dramatic illustration is offered by Jansky's discovery observations of the radio signals from the center of the Milky Way, a region forever forbidden for visual observation because of intervening celestial clouds.

One last general point will be made before we turn our attention to some specific results from radio astronomy and to the instruments that make such results possible. What is the nature of the radio signal from celestial sources? First, it is a weak signal, very weak by the standards of communication engineers. The energy continually coming from a relatively strong celestial source amounts to no more than 1 watt of power over the entire area of the earth. A typical radio astronomy telescope in use today must deal with one billionth of a billionth watt

(0.000,000,000,000,000,001 watt). The mile-size telescope previously mentioned, because of its much greater collecting area, would offer a ten thousandfold improvement, which astronomers would apply immediately to the observation of sources now too faint to be detected with certainty.

Celestial radio signals are static; in communication terms, the modulation is completely random – pure "white" noise familiar as a steady hiss in earphones, or as the "snow" on a radar screen. The variation of signal strength or intensity with wave length is sometimes so sharp or pronounced that a particular wave length or frequency can be ascribed to the celestial source. In other cases, the radiation is said to be "thermal" because it covers the observable spectrum with only gradual variation. In relatively rare cases, the celestial signal may be partially polarized, which indicates that some phenomenon at the celestial source causes the individual radiators to prefer some particular orientation.

In the ten years immediately following Jansky's discovery, almost the only person who pursued the matter was another United States citizen, Grote Reber,[2] who built the first true radio telescope and extended Jansky's observations into a survey or plot of the Milky Way. However, the advances in electronic techniques during World War II led to a considerable number of intentional or chance radio astronomy observations with radar equipment and, by 1950, radio astronomy programs were under way, particularly in Australia, England, and the Netherlands. In the last decade the body of radio astronomy knowledge has grown rapidly and the rate is still increasing. What has been learned?

The sun emits radio signals, a portion of which is fairly constant from day to day, and other portions presumably related to solar flares and sun spots may vary rapidly, by factors as large as a thousand. If the sun were removed to the distance of the nearer stars, we should not be able to detect solar radio emissions with present equipment. Neither have normal stars been detected by radio, but larger telescopes and more sensitive receivers are being developed, and some day soon it may be possible to make these observations.

The moon and some of the planets have been observed by radio. Venus appears to be warmer than expected, even if allowance be made for the greenhouse effect of the heavy atmosphere. Jupiter emits in a most curious fashion. Burke and Franklin[3] discovered extremely energetic bursts in a narrow wave-length band centered at about 50 feet. The bursts do not occur at all times and the source, whatever it is, partakes of rotational motion that slips a little with respect to the rate observed for the equatorial belt of Jupiter. Furthermore, at other shorter wave lengths, Jupiter emits in a fashion that cannot be explained by a simple hot body or thermal source; it has been suggested by Drake[4] that we are observing on Jupiter the equivalent of the Van Allen belts recently discovered around the earth.

A majority of the radio sources thus far discussed has not been identified with objects that can be observed visually. Where such identifications have been made, however, the object usually involves dust or gas clouds in violent motion. Typical sources of radio signals are the interstellar clouds that visual astronomers had previously plotted. Such sources are not mere points in the sky, like a star, but cover large angular patches and actually fill enormous volumes of space. An unusual source is the Crab Nebula, which is composed of the remnants of a star that exploded in 1054 A.D., as recorded by Chinese astronomers. The dust and gas are still in a very turbulent condition, expanding outward from the position of the former star.

Hydrogen gas in its neutral state may emit (or absorb) at a radio wave length of about 8 in. (21 cm., or a frequency of 1420 mc./sec.). This emission is as characteristic of hydrogen as the 2 well-known visual yellow lines are characteristic of sodium. Detailed studies of the hydrogen emission, particularly by astronomers in the Netherlands and Australia, have shown that the hydrogen in our Milky Way system is not smoothly distributed, but is concentrated in long streamers or arms suggestive of the structure we can observe visually in other galaxies.

These external galaxies can be detected at radio wave lengths. It is difficult to study the structure of the Milky Way from within, and a better understanding of the mechanisms involved perhaps may be obtained more easily from a study of the Andromeda nebula, which is sufficiently close to permit such studies with instruments now in operation or technically feasible.

The most powerful radio emitter which we know is found in the constellation Cygnus. Visually, the source is too faint for observation except with the largest instruments. Apparently, two galaxies are in collision. The consequences of this process exceed anything we could have imagined, and the signal we receive here on the earth is exceeded in intensity by only one other, which comes from a radio source located nearby in our Milky Way. If the Cygnus source were removed so far as to be at the limits of our radio astronomy equipment, the colliding galaxies would be too faint to be observed visually, which has given rise to the comment that radio astronomy can penetrate deeper into the universe than visual observations, and thus holds a major promise for contributing to the solution of the riddles of the universe – the balance between energy and matter and the limits of time and dimension that may apply.

There are some radio observations that can be made with relatively simple equipment. However, most of the research programs today make use of instruments that were not available even a few years ago. Steady progress must be accompanied by instrumental developments that challenge the best structural, mechanical, and electronic engineers.

The existence of the hydrogen emission at 1420 mc./sec. was predicted by van de Hulst[5] in the early 1940s, but it was not observed for almost 10 years, awaiting the development by Ewen and Purcell[6] of a receiver with the requisite sensitivity. Today, observation of the hydrogen line is quite commonplace. Meanwhile, the invention of traveling-wave tubes, parametric devices, and the maser promises another magnitude of improvement in receiver performance.

Although special radio telescopes were built at a few places in the late 1940s, of which the precision 50-foot paraboloid at the Naval Research Laboratory, Washington, D.C., is an example, the real incentive for better telescopes stems from the decision by Lovell and his associates in England to build the giant 250-foot paraboloid now in operation there.

In the United States, the year 1954 marked a turning point for radio astronomy. It was then clear that research there would require improved instruments if progress were to keep pace with that in other countries. The National Science Foundation in Washington, D.C., in particular, initiated steps that ultimately led to the establishment of the National Radio Astronomy Observatory at Green Bank, W. Va.[7] At the outset, the decision was made that this research institution would be equipped with instruments of the most advanced type, particularly in those cases where costs were so great as to discourage purchase by any one college or university engaged in radio astronomy. Consequently, the National Radio Astronomy Observatory is operated in a manner to encourage scientific visitors. Since the new observatory started observations with the Howard E. Tatel 85-foot telescope, visiting scientists have come not only from within the United States, but also from other countries, to take advantage of some of the unique research facilities at Green Bank.

A horn 120 feet long has been built as part of the NRAO program for the standardization or calibration of radio-astronomy observations. A precision telescope with a 140-foot paraboloid is being constructed. The navy is building a 600-foot parabolic telescope at Sugar Grove, W. Va., about 30 miles east and north of Green Bank. Some of the time on this instrument will be made available for astronomical research; therefore, plans at Green Bank are looking ahead to the construction of a telescope with an aperture of about one-half mile, this gain being attained by sacrificing sky coverage and restricting it to a small zone a few degrees each side of the zenith, perhaps similar in concept to the 1000-foot telescope now being planned by Cornell University, Ithica, N.Y., under a Department of Defense contract.

There are no sharp boundaries between the domains of geophysics, space, and radio astronomy. Similar, if not identical, research instruments are used for studying the upper atmosphere and for the exploration of the solar system by means of radar techniques. Astronomical techniques or methods may be utilized as tools in achieving the goals of a space

probe; conversely, a space satellite may offer astronomy an observing station free of many of the limitations imposed by our atmosphere.

We may soon face instrumental limitations as critical as those of 1954. A way to remove these limitations in the most effective and efficient manner will emerge from the joint efforts of astronomers, engineers, and other scientists. It is certain that the next few years will witness startling instrumental innovations that will call for the same imagination, courage, and conviction that fostered the giant telescope at Jodrell Bank more than a decade ago.

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DIVISION OF BIOCHEMISTRY

PROPERTIES OF HEART MUSCLE CYTOCHROMES PREPARED WITH DEOXYCHOLATE*

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The first use of a surface active agent to solubilize an intracellular constituent was probably that by Kühne,[1] who employed bile salts in 1879 to obtain rhodopsin from the retina of the eye. The specific use of deoxycholate may have begun with the work of Alloway,[2] who extracted the transforming principle of pneumococcus. Although Hopkins *et al.*[3] in 1939 employed deoxycholate to prepare succinate-methylene blue reductase and Keilin and Hartree[4] used the same agent to "peptize" heart muscle particles so as to make them transparent for spectroscopic examination, the more extensive use of deoxycholate began in 1947 when we separated cytochrome c oxidase from the heart muscle mitochondrial fragment.[5] Previously, Straub[6] and Yakushiji and Okunuki[7] had solubilized the same enzyme with sodium cholate.

The property of deoxycholate to solubilize many unrelated compounds is probably related to its ability to react with both lipid- and water-soluble substances. It is generally agreed that one side of the deoxycholate molecule presents a nonpolar front and the other a polar front (FIGURE 1). This dual nature also is considered to be responsible for its ability to form micelles and gels, that is, to react with itself to form aggregates.

Among the unusual reactions of deoxycholate is its ability to form choleic acids. These are addition compounds with some acids, esters, ethers, phenols, and hydrocarbons. Apocholic acid is apparently the only other substance known to share this property to the same degree. X-ray diffraction studies indicate that choleic acids are compounds in which the deoxycholate is so arranged as to leave a cylindrical hole into which the other substance fits.[8] The deoxycholate fences in the second component without benefit of covalent bonding.

Whether phospholipids form choleic acids is not known at this time. However, this is the assumption made by Verschure *et al.*,[9] who found an electrophoretically homogeneous complex formed between soya bean or egg yolk lecithin and deoxycholate at *p*H 8.6 in barbital buffer. The complexes had a mean electrophoretic mobility of 8.8×10^{-5} cm.^{2} sec.$^{-1}$ and a mean sedimentation constant of 2.2×10^{-13} sec. M. Reich and W. W. Wainio (unpublished data) also have shown by equilibrium dialysis

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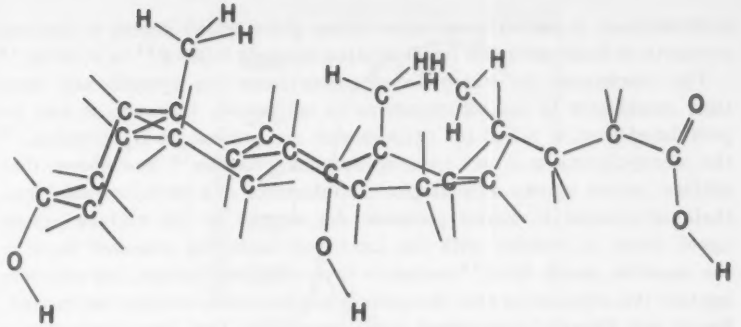

FIGURE 1. The structure of deoxycholic acid. Most of the hydrogen atoms have been omitted to expose the nonpolar (CH_3) and polar (OH) fronts.

and electrophoresis that there is a complex formed between phosphatidylethanolamine and deoxycholate. The nature of the binding is not known.

Deoxycholate also is able to form complexes with proteins. For example, from a plot of deoxycholate binding by albumin as a function of the free acid Rudman and Kendall[10] calculated that the maximum number of anions bound per molecule of albumin is 12. From the *p*H dependence of the binding it was assumed that the deoxycholate is attached to the ϵ-animo groups of lysine. Rowley and Wainio[11] also have determined that the number of deoxycholate anions bound by a molecule of cytochrome c is 17 (as determined by electrophoresis) or 12 (as determined by equilibrium dialysis). The first value is probably high due to the presence of free deoxycholate, which could not be estimated accurately, and both figures are to be compared with the value of 13, which is the excess number of positive charges on cytochrome c at the *p*H of the experiments, namely, 8.55. It follows, therefore, that the binding of deoxycholate to lipid-free proteins is of the electrostatic type.

Being a surface-active agent, deoxycholate shares the property of forming micelles. McBain[12] and other investigators have postulated that whenever micelles are formed there are two types of aggregates in solution. One is a large "neutral" colloid that appears to have a laminated structure and contributes nothing to the conductivity, while the other is a highly charged ionic micelle that is spherical and much smaller in size. The latter is assumed by some[13] to be able to dissolve fats. Bile salts do not appear to incorporate long-chain alcohols into palisade layers,[14] which might indicate that only the ionic micelle exists in deoxycholate solutions. In the spherical micelle the lipophilic groups would be oriented toward the interior, while the polar groups would be directed toward the exterior and thus disperse the particles in the aqueous medium. No association of deoxycholate molecules is assumed to occur up to a concentration of about 0.005 *M*. Above this

concentration a partial association takes place which seems to become complete at least when the concentration exceeds 0.008 *M*[15] or 0.010 *M*.[16]

The mechanism by which deoxycholate frees the cytochromes from their attachment to the mitochondrion is not known. However, it may be postulated that, if all of the cytochromes are present as lipoproteins,[17] the deoxycholate may act by displacement. Tayeau[18] has shown that surface active agents will displace cholesterol and phospholipids from their attachment to serum proteins. An excess of the surface active agent forms a complex with the lipid and holds the released lipid in the aqueous phase. Gurd[19] seems to favor this mechanism, but cautions against the assumption that the protein configuration remains unchanged. Reich and Wainio (unpublished data) have found that deoxycholate will displace phosphatidylethanolamine from its attachment to cytochrome c, with which it forms a complex.

It may be suggested then that the deoxycholate disrupts the lipoprotein structure of the mitochondrion by displacement, that is, the deoxycholate substitutes for the lipid molecules of the cytochrome-lipoprotein and thus frees the latter. The detached cytochrome-lipoprotein becomes soluble by virtue of the polar groups of more deoxycholate molecules that complex with the lipid of the cytochrome-lipoprotein and become directed toward the aqueous phase. The cytochrome-lipoproteins are probably too large to be engulfed as choleic acids and the protein-binding of deoxycholate is too small to overcome the hydrophobic properties of the lipid of the molecule. A special property of deoxycholate that it does not share with any of the other bile salts[20] is its ability to detach sequentially the cytochrome-lipoproteins to such an extent that they can be separated by centrifugation.[21]

The use of deoxycholate to solubilize the cytochromes is offset to some degree by two disadvantages: one is the tendency of deoxycholate to form a gel; the other is the inhibitory action of deoxycholate. When acid is added to an aqueous solution of sodium deoxycholate the solution becomes extremely viscous below *p*H 6.6. In fact, if the solution is concentrated sufficiently, the gelation can occur at *p*H 7.4, but rarely at 8.4. Rich and Blow[22] have studied the acid-gel and, after drawing it out into long, glassy fibers that dry into clear, brittle rods, they find by X-ray diffraction that the deoxycholic acid forms helical complexes of macromolecular dimensions. Sodium cholate, sodium lithocholate, and several other bile salts do not form similar helical complexes.

The inhibition of enxyme activity by deoxycholate is by far the greater disadvantage of its use. When increasing amounts of deoxycholate are added to heart muscle particles, the activities of two enzyme systems (FIGURE 2) first increase and, after having reached a maximum, decrease again (M. T. Spoerlein and W. W. Wainio, unpublished data). In the instance of the reduced diphosphopyridine nucleotide-cytochrome c reductase activity there is no rise, and the activity decreases to almost

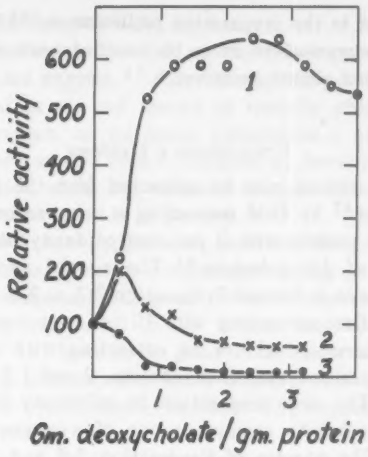

FIGURE 2. The effect of an increase in the deoxycholate:protein gram ratio on the activities of three enzyme systems: (1) cytochrome c oxidase; (2) succinate-cytochrome c reductase; and (3) DPNH-cytochrome c reductase.

zero. Inhibition can also be demonstrated by adding deoxycholate to a soluble preparation of cytochrome c oxidase.[23] The inhibition is found to increase with increasing concentration of deoxycholate and to increase with increasing time of contact of the deoxycholate with the enxyme. It can be shown by removing the deoxycholate with resin from a cytochrome c oxidase preparation (FIGURE 3) that even the

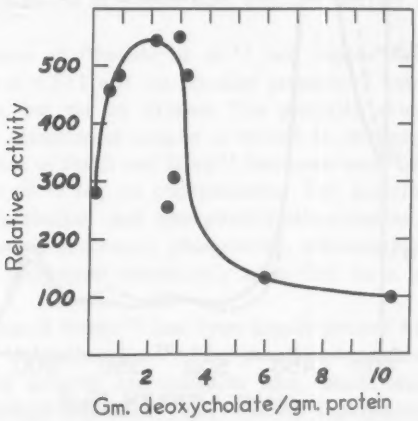

FIGURE 3. The effect of a decrease in the deoxycholate:protein gram ratio (obtained with Amberlite XE-98 resin) on the relative activity of a soluble cytochrome c oxidase preparation.

deoxycholate used in the preparation is inhibitory.[24] However, complete removal of the deoxycholate is to be avoided because the enzyme becomes insoluble and almost inactive.

Cytochrome c Oxidase

Cytochrome c oxidase may be extracted from the heart muscle mitochondrial fragment[25] by first extracting a suspension of particles containing 25 mg. of protein with 2 per cent of deoxycholate and then with 2 or 3 per cent of deoxycholate.[21] The second supernatant fluid that contains the oxidase is termed Preparation 2-2 or 2-3. Other preparations may be made by first extracting with 10 per cent methanol (Preparation 10 per cent methanol-2-3),[24] or by extracting with 4 per cent cholate between two extractions with deoxycholate, 2 and 1.5 per cent (Preparation 2-4-1.5).[26] The last preparation is relatively inactive unless the 2 per cent deoxycholate extract or one of a number of phospholipids is added to it. The spectra of Preparation 2-2 and Preparation 2-4-1.5 in the reduced state are given in FIGURE 4. The latter is the purer

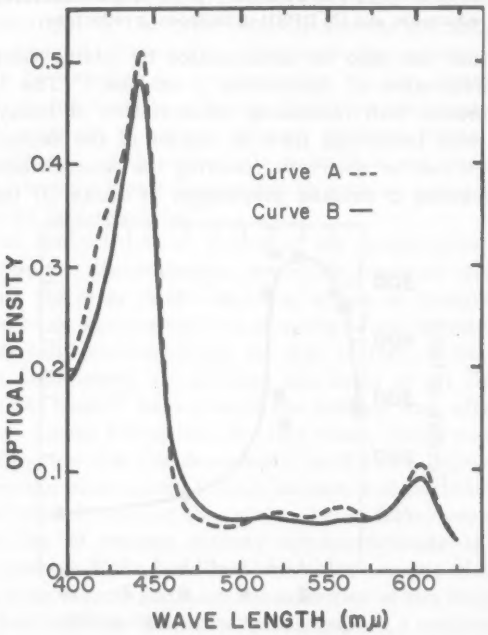

FIGURE 4. Spectra of two preparations of beef heart cytochrome c oxidase in the reduced state; curve A, Preparation 2-2; curve B, Preparation 2-4-1.5, Reproduced by permission of *The Journal of Biological Chemistry*.

preparation, as judged spectrally.

The oxidase in Preparation 2-3 oxidizes ferrocytochrome c and is itself reduced by this enzyme.[27] After having been reduced, the oxidase is rapidly oxidized in air and serves to transfer electrons from ferrocytochrome c to oxygen, as its name, cytochrome c oxidase, indicates. The oxidized enzyme can be readily reduced by ferrocytochrome c in the presence of cyanide, while the reduced enzyme can be oxidized only very slowly in air when cyanide is present.[28]

Preparation 2.05-2 has copper and heme in the ratio 1.6:1, while Preparation 2-4-1.5 has the same constituents in the ratio 1:1. Fractions made from heart mitochondrial fragments with deoxycholate have copper: heme ratios ranging from 0.8:1 to 1.9:1 when the copper is determined spectrographically.[29] There is a good correlation in these fractions between the copper content, the heme content, and the activity (with a lipid activator) of cytochrome c oxidase. The copper may be removed and the activity proportionately decreased by dialysis for 12 hours against a number of reagents as, for example, against sodium diethyldithiocarbamate. Preliminary studies indicate that the copper is mostly in the cuprous state in the air-oxidized enzyme.[30] The tentative conclusion is that the copper does not participate in electron transfer, but acts simply to bind the oxygen to or near the electron-transferring heme site.

Other soluble preparations are those of: (1) Yakushiji and Okunuki[7] as modified by Okunuki *et al.*;[31] (2) Smith and Stotz[32] as modified by Connelly *et al.*;[33] and (3) Mackler and Penn[34] as modified by Hatefi.[35] All of these preparations depend on the use of cholate as a solubilizing agent. The preparation of Hatefi also employs tertiary amy alcohol and deoxycholate.

The preparation of Okunuki *et al.*[31] has copper and iron in the approximate ratio of 4.5:1 and the peculiar property of being fully oxidized by ferricyanide, but not by oxygen. The partially oxidized preparation obtained in the presence of oxygen is termed an oxygenated preparation.

The preparation of Smith and Stotz[32] has been most carefully analyzed by Marinetti *et al.*[36] for its phosphatides. The principal phosphatides are phosphatidylcholine and phosphatidylethanolamine, and there are substantial amounts of inositol phosphatide, phosphatidylserine, spingomyelin, and a component tentatively identified as a polyglycerophosphatide.

The preparation of Hatefi[35] has been depolymerized with thioglycolate by Ambe and Venkataraman.[37] The resulting preparation requires a phospholipid for activity and contains iron, heme, and copper in the ratio 1:1:1. Criddle and Bock[38] have further depolymerized the oxidase with sodium dodecyl sulfate (which shifts the α-maximum of the reduced enzyme from 603 mμ to 595 mμ) and report a molecular weight of 72,000 for the monomer.

Cytochrome b

Cytochrome *b* may be obtained from the mitochondrial fragment by extracting with 0.6 and then 0.8 per cent deoxycholate. After 4 hours at 168,000 g, the second supernatant fluid, Preparation 0.6-0.8, yields a red gelatinous pellet that can be solubilized with phospholipase A. The obvious contaminant, cytochrome c_1, can be removed by first adding crude pancreatic protease and by then fractionating with ammonium sulfate.[39]

The resulting preparation has the spectra given in FIGURE 5. The reduced enzyme has maxima at 430, 532, and 562 mμ. These peaks cannot be obtained with succinate, since the preparation has no succinic dehydrogenase activity, nor can any cytochrome c oxidase activity be detected. In other words, the cytochrome *b* apparently is enzymatically inert, although its inertness may be due to an absence of the proper electron donor and acceptor and/or cofactors.

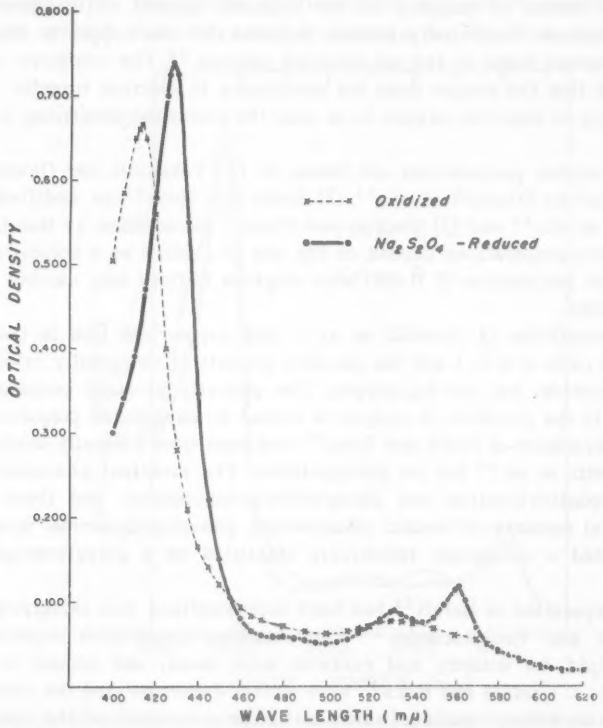

FIGURE 5. Spectra of beef heart cytochrome *b*. Reproduced by permission of *Science*.

The redox potential of cytochrome *b* has been elevated in recent years from the value of –40 mv first determined by Ball[40] to a value of near zero mv[41] and then to +77 mv.[42] Our value, obtained with the soluble preparation, is +68 mv (D. Feldman and W. W. Wainio, unpublished data).

Sekuzu and Okunuki[43] claim a crystalline preparation of cytochrome *b* with a redox potential of –50 mv. This preparation was obtained by the use of cholate and by ammonium sulfate fractionation, both before and after treatment with a bacterial proteinase. No details, other than the spectrum, are available.

Cytochrome c_1

Cytochrome c_1 can be prepared from heart muscle mitochondrial fragments by the following procedure.[44] A suspension of particles is washed for 21 hours in dilute buffer and then "aged" for 48 hours in the cold. The particles are concentrated and extracted with 1 per cent deoxycholate. The extract is allowed to stand for 30 hours in the cold to destroy more of the cytochrome *b*. After clarification and lyophilization, the reconstituted preparation is treated with 10 per cent ammonium sulfate. The supernatant fluid is dialyzed against phosphate buffer, and Amberlite IRC-50 is used to remove the remaining cytochrome *c*.

The spectrum of the reduced enzyme is presented in FIGURE 6. It has maxima in the reduced state at 418, 523, and 553 mμ, which correspond to those already in the literature. Although the most persistent

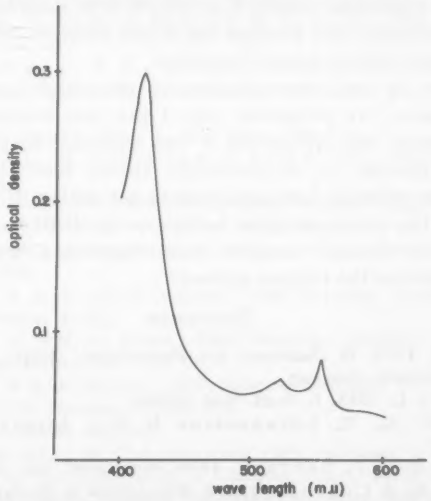

FIGURE 6. Spectrum of beef heart cytochrome c_1 in the reduced state.

contaminant is a small diaphorase activity, the enzyme itself is almost enzymatically inert. However, it will slowly oxidize reduced diphosphopyridine nucleotide (DPNH) aerobically, and will also enhance the slow anaerobic oxidation of DPNH in the presence of fumarate as an electron acceptor when a particulate preparation from heart muscle is added as an enzyme system.

Green *et al.*[45] have prepared cytochrome c_1 by using deoxycholate, butanol, ammonium sulfate, Duponol, and cholate. The redox potential is +223 mv, and it will not replace cytochrome c in any of the systems in which it has been tested. The enzyme contains 14.7 μmoles of heme and 0.82 μmoles of flavin per mg. of protein, and no lipid.

Summary

The surface active agent deoxycholate has properties that are not present to the same degree in the other bile salts. It can sequentially detach the cytochromes contained in the heart muscle mitochondrion so that they can then be separated by centrifugation. It can also solubilize these cytochromes, which are apparently detached as lipoproteins. The most probable mechanism of detachment is replacement, and the most probable mechanism of solubilization is complex formation with the lipid.

Cytochrome c oxidase prepared with deoxycholate has been shown to be a lipid-containing copper-heme-protein and, in fact, one requiring a phospholipid for its activity.

Cytochrome *b* has been prepared with deoxycholate, phospholipase, protease, and ammonium sulfate. Cytochrome *b* is apparently enzymatically inert, but probably only because the proper electron donor and acceptor and/or cofactors have not been identified.

Cytochrome c_1 has been prepared by prolonged washing to remove the cytochrome c, by extraction with 1 per cent deoxycholate, and by aging to destroy the cytochrome *b* and succinic dehydrogenase. This preparation likewise is enzymatically almost inert. However, it can slowly oxidize reduced diphosphopyridine nucleotide (DPNH) aerobically and enhance the slow anaerobic oxidation of DPNH in the presence of fumarate as an electron acceptor when fragmented heart muscle mitochondria constitute the enzyme system.

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DIVISION OF MICROBIOLOGY

IMMUNITY TO COCCIDIOIDOMYCOSIS INDUCED IN MICE BY PURIFIED SPHERULE, ARTHROSPORE, AND MYCELIAL VACCINES*

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The micromorphology of *Coccidioides immitis* is determined, in large measure, by its growth environment. The fungus is clearly dimorphic and assumes usually, but not exclusively, the sporangium or spherule form in the living host. On conventional laboratory media the growth consists of a septate mycelium which, in time, fragments to form arthrospores.

However, numerous workers (see Fiese, 1958) have reported the sporadic occurrence of spherules in specialized lifeless media. The nutritional and physicochemical factors influencing their occurrence have been studied by Converse (1955, 1956, 1957) and Converse and Bessemer (1959), who formulated chemically defined media that favored spherule formation from arthrospore inocula. This important development has made it possible to compare the immunizing properties of the spherule-endospore structures with those of other morphologic elements.

The relevance of such a comparison in the potential development of a coccidioidal vaccine is suggested by certain relationships between morphologic form and infectivity or pathogenesis. Whereas it is primarily the spherule form that parasitizes the host, coccidioidal infection is initiated in nature by the arthrospore form. Therefore, knowledge of possible differences in immunogenicity between these forms appears to be pertinent to the problem of prophylactic immunization. Similarly, information on the relative immunogenic attributes of the mycelial phase is important because the latter possesses antigens involved in the dermal sensitivity, precipitin, and complement-fixation reactions.

This paper describes certain aspects of protective immunity induced in mice by formalin-killed and purified mycelial, arthrospore, and spherule-endospore vaccines, respectively. Techniques by which the spherules and endospores were produced and separated from other structures are described.

Methods

Mycology. The Silveira strain (Friedman *et al.*, 1956) of *C. immitis*, isolated in 1951 from a severe primary human coccidioidal infection, was

*This paper, illustrated with slides, was presented at a meeting of the Division on March 25, 1960. The work was supported by the Bureau of Medicine and Surgery, United States Navy, and by the Office of Naval Research, Washington, D.C., under a contract with the Regents of the University of California. Opinions contained in this report are not to be construed as reflecting the views of the naval service.

employed throughout. The culture was maintained on glucose yeast-extract agar (GYE, Friedman *et al.*, 1953) by transfer twice yearly. It was of high virulence for the Namru mouse (Garber and Hauth, 1950), which served as the host in these studies.

Homogeneous crops of arthrospores (FIGURE 1) were obtained by the suction harvest technique described by Friedman *et al.* (1956) after growth of the fungus at 37° C. for 4 to 6 weeks on GYE agar. The dry

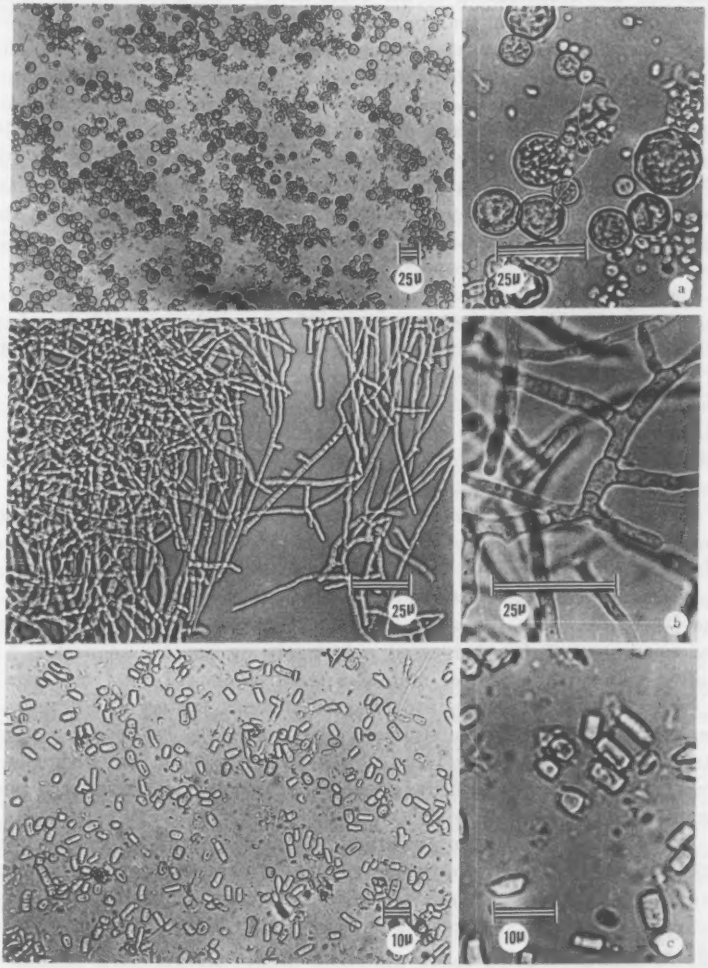

FIGURE 1. *(a)* Purified spherule endospore, *(b)* mycelial, and *(c)* arthrospore preparations. All preparations in 0.85 per cent NaCl, unstained.

material was then suspended in distilled water at a concentration of approximately 10^8 organisms/ml. and aliquots were refrigerated for subsequent challenge or inoculation of media. The remainder of the arthrospore suspension was sterilized by the addition of a final concentration of 0.5 per cent formalin (vol./vol.) that remained in contact with the organisms for a minimum of 8 to 14 days at 3° C. The arthrospores were subsequently washed with water or saline by centrifugation, concentrated and standardized on the basis of dry weight for immunization.

Two lots of mycelial antigen were employed. The first was prepared from 3-day-old shake cultures incubated in GYE medium at 37° C. The fungal growth was harvested by filtration, washed with distilled water, sterilized as above, rewashed, and resuspended in water. The second lot was prepared from 48-hour-old shake cultures incubated in a defined medium (Basal No. 2 broth, Roessler *et al.*, 1946) modified by the addition of 2 per cent mannitol and the omission of glucose. This innovation was found to delay arthrospore formation. As a consequence, the mycelial antigen, harvested after 48 hours of growth, was microscopically free (FIGURE 1) of arthrospores.

The spherule-endospore phase was produced in the BSM medium of Converse (1957) modified to contain 25 per cent more acid phosphate (BSM-1). It was found with strain Silveira, however, that high yields of spherules (TABLE 1) were attainable consistently only when purified and concentrated 3- to 5-day-old endospore inocula were employed. Since the preparation of an endospore inoculum was dependent, in turn, on the prior production and rupture of spherules, the procedure described below was utilized to obtain the endospore phase.

Numerous replicate flasks containing BSM-1 were inoculated with viable arthrospores to give a concentration of 10^6/ml. Those flasks that after incubation at 37° C. for 2 to 3 days showed 30 per cent or more spherulation were incubated further until there was extensive rupture of the spherules (usually after 2 to 3 additional days). The released endospores were then harvested selectively by aseptic sequential filtration through 2 layers of stainless steel screen (1-mm.^{2} openings), 8 layers of surgical gauze, and 8 layers of nylon hosiery (51 gauge, 15 denier) and twice through a stainless steel screen (120 μ^2 openings) constructed of 50-μ-diameter wire. Following filtration, the endospores were concentrated by centrifugation and suspended in saline at a concentration of approximately 10^8/ml.

The filtered endospores (FIGURE 2) served as inoculum for fresh BSM-1, and the fungal growth was treated as above. The procedure was repeated 5 to 8 times (total) to provide sufficient endospores for inoculation of the production medium (BSM-1) with a final concentration of 10^6 endospores/ml.

The harvest consisted primarily of spherules and endospores, but hyphal strands were invariably present. After sterilization with formalin

TABLE 1

EFFECT OF INOCULUM ON SPHERULE FORMATION BY *COCCIDIOIDES IMMITIS* STRAIN SILVEIRA

Inoculum			*Spherule medium*	*No. replicates showing spherulation at indicated levels (%)*			
Medium	*Morphology**	*Age in days*		<30	>30	>60	>90
Basal #2 broth	My-Hf-As	3-5	BSM	2			
	Hf-As-My	6-8		22	2		
	As-Hf-My	9-18		16			
	As-Hf-My	19-28		8		2	
GYE broth	As-Hf-My	3-8	BSM	14**	2		
GYE agar	As	7-20	BSM	8	6		4†
	As	21-41		16	4†		4
BSM	Es	3-5‡	BSM	10			
	Es	3-5				2	4
	Es	6-8			2	4	
BSM-1	Es	4-5‡	BSM-1	2			
	Es	3-4			4	12	16§
	Es	4-5				2	187

Key: *Mycelium (My), hyphal fragments (Hf), arthrospores (As), and endospores (Es) listed in decreasing order of abundance from left.

**Two of the 14 replicates were inoculated with washed cells.

†Glutathione 0.003 *M.*, added to 2 of the 4 flasks of medium.

‡Filtered only as described in text; all other inocula containing endospores were both filtered and concentrated to provide the initial viable concentration described in text.

§Glutathione 0.003 *M.*, added to 5 of the 16 flasks of medium.

as described above, the strands were removed by 5 to 10 cycles of filtration through glass wool, and this resulted in a preparation (FIGURE 1) that contained approximately 1 short hyphal strand per 10^3 to 10^4 spherules and endospores. The filtration procedure resulted in losses of spherules and endospores estimated to exceed 90 per cent.

Recently it was observed that after centrifugation (1300 g, 30 min.) of a mycelium-containing preparation of spherules (FIGURE 3*a*) layered on 80 per cent (wt./vol.) aqueous sucrose solution, the sediment consisted primarily of spherules and endospores (FIGURE 3*b*). The immunizing properties of spherules purified by this method have not yet been determined.

Immunity. The vaccines were assayed by determining their capacity to protect mice against graded challenge doses of arthrospores. At the inception of an experiment the mice (female) were 6 to 8 weeks of age and weighed between 20 and 30 gm. Following one or more administra-

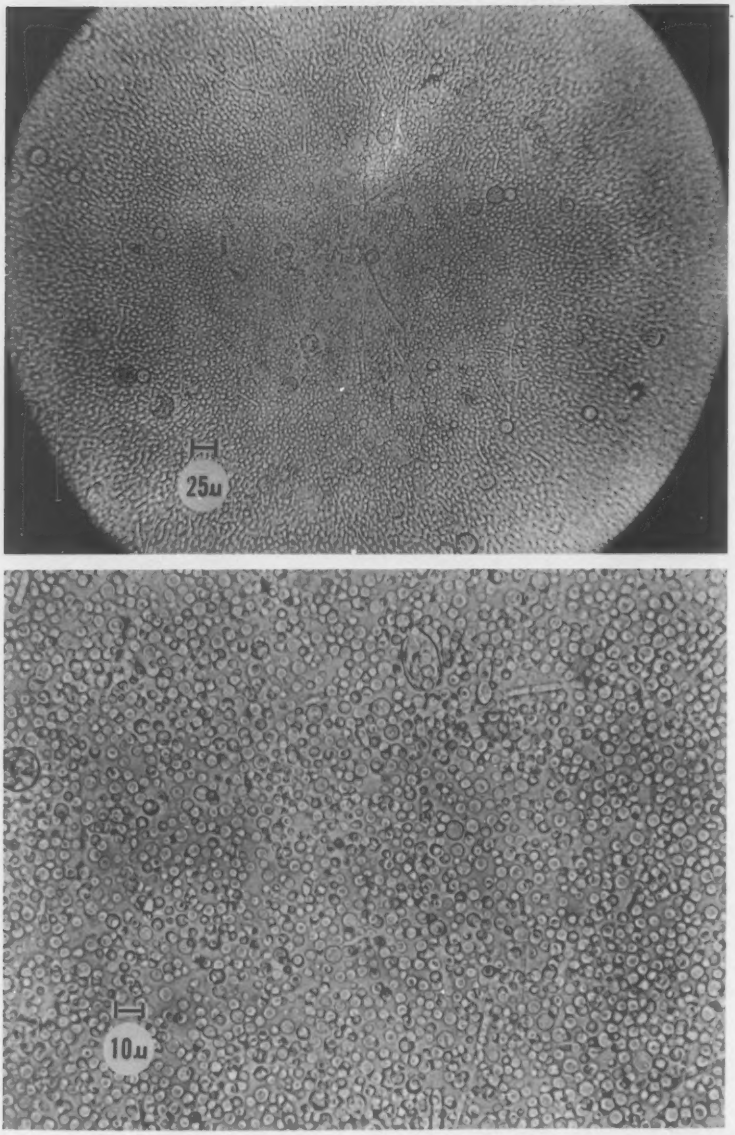

FIGURE 2. Purified endospore inoculum. Preparation in 0.85 per cent NaCl, unstained.

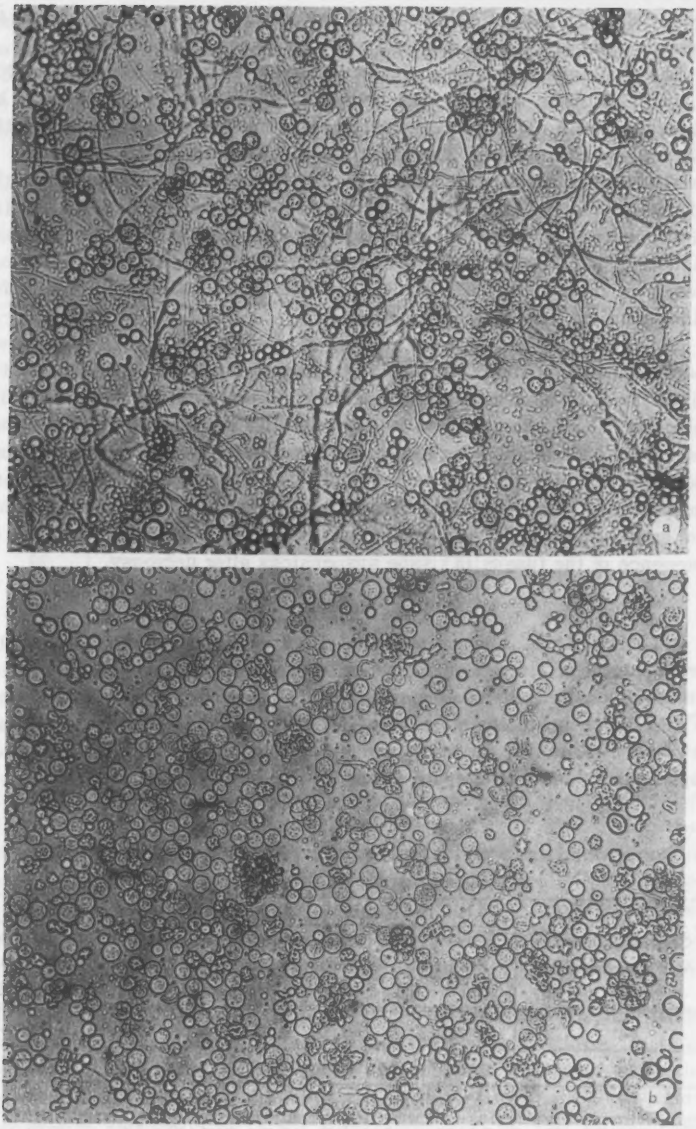

FIGURE 3. Effect of centrifugation through 80 per cent sucrose on the removal of mycelium from spherule-endospore preparations: *(a)* before treatment; *(b)* after treatment.

tions of 0.05 ml. of the vaccines by the routes described later, the animals were challenged at 3 to 5 weeks after the last booster.

The challenge doses were always administered by the intranasal (INA) route. This route was selected because Pappagianis *et al.* (1960) had observed that a significant percentage of mice that were immune to lethal challenge administered intraperitoneally succumbed to the same or smaller doses administered intranasally. It was believed, therefore, that challenge via the INA route represented a more severe and critical test of immunity than parenteral challenge notwithstanding its inherent limitation with regard to precise quantitation. The former route is also more nearly equivalent to the route of exposure in natural coccidioidal infections than are the parenteral routes.

INA challenge or, in some cases, vaccination by the INA route was performed by instilling 0.05 ml. of the preparation intranasally in anesthetized mice. Control mice were inoculated in the same manner with saline placebo. The challenge dose is expressed as the number of arthrospores per dose, although it is recognized that the number of arthrospores actually reaching the lung is lower. The viable content of the challenge suspensions was determined by pour plate assay of appropriate dilutions in agar (Roessler *et al.*, 1946). Malt agar was used to determine the presence of the fungus in tissue suspensions after necropsy.

Results

TABLES 2 and 3 summarize the effect of intramuscular immunization with a total of 1.6 mg. of each vaccine on mortality and residual lesions in mice challenged subsequently with *C. immitis*. Challenge doses of 79 to 318 arthrospores were lethal for 80 to 90 per cent of the untreated animals within 20 days. In the group inoculated with formalin-killed spherules, there was 1 death among 29 mice challenged with these doses

TABLE 2

IMMUNOGENICITY OF FORMALINIZED SPHERULES, ARTHROSPORES, AND MYCELIUM OF *COCCIDIOIDES IMMITIS*[*]

Challenge dose (No. arthrospores)	*Dead/total at 20 and 105 days postchallenge*							
	Control		*Spherule-vaccinated*		*Arthrospore-vaccinated*		*Mycelium*[†] *vaccinated*	
	20	105	20	105	20	105	20	105
44	2/10	3/10	0/10	0/10	0/10	0/10	0/9	0/9
79	8/10	8/10	0/10	0/10	2/10	2/10	3/10	6/10
127	9/10	10/10	0/10	1/10	4/10	5/10	2/10	2/10
318	9/10	9/10	0/9	0/9	4/10	4/10	3/10	3/10

[*] Vaccine dosage: 0.8 mg. inoculated intramuscularly on each of days 1 and 8; animals challenged by the intranasal route on day 29.

[†] Lot 2.

and observed for 105 days (TABLE 2). At autopsy (TABLE 3), 71 per cent of the survivors in this group still harbored *C. immitis*, but gross lesions were absent in 47 per cent of the survivors. In the remainder, pulmonary lesions were primarily discrete (1 to 3 mm. in most animals). There was no evident pathological involvement of the liver or spleen in any of the spherule-immunized mice; however, *C. immitis* was cultured from one or the other of these organs in 5 animals.

TABLE 3

MORTALITY AND SEQUELAE IN IMMUNIZED AND CONTROL MICE SACRIFICED AT 105 DAYS POSTCHALLENGE*

Challenge dose (range)	*Mortality and autopsy findings*	*Control*	*Vaccinated with*		
			Spherules	*Arthrospores*	*Mycelium*
44 to 318	Per cent mortality	75	3	28	28
	No. survivors autopsied	10	38	28	26
	Per cent survivors with:				
	No lung lesions	70	47	43	35
	Minor lung lesions	0	53	50	35
	Advanced lung lesions	30	0	7	30
	Liver and/or spleen lesions	20	0	4	31
	Positive cultures	30	71	79	69

*See TABLE 2 for immunization schedule and challenge details.

In those groups vaccinated with formalin-killed arthrospores or mycelium, the mortality ratio after challenge (TABLE 2) was higher than among the spherule-immunized animals, but lower than in the control group. Lesions in the lung and other organs were generally more marked in the arthrospore-vaccinated survivors than in the spherule-vaccinated group and increasingly so in the mycelium-vaccinated group (TABLE 3). In the latter group almost one third of the survivors showed foci of infection in the liver or spleen or both.

The mycelial vaccine also induced lesser immunity to the lethal disease than the spherule vaccine when both were employed in total doses of 4.5 to 6.0 mg. administered either by the INA route or by the combined INA and subcutaneous (SC) routes (TABLE 4). In other experiments (unpublished) the immunogenicity of the formalinized mycelium (1.5 mg., intramuscularly) was not improved by emulsification in a cholesterol-peanut oil adjuvant.*

*Pendil, Endo Products, Inc., Richmond Hill, N.Y.

TABLE 4

IMMUNOGENICITY OF FORMALINIZED ARTHROSPORES AND MYCELIUM OF *COCCIDIOIDES IMMITIS*

Challenge dose (no. arthrospores)	*Dead/total at 90 days postchallenge*					
	Control	*Spherule-vaccinated*			*Mycelium*-vaccinated*	
		*4.5 mg. SC***	*6.0 mg. SC-INA†*	*4.5 mg. INA‡*	*6.0 mg. SC-INA†*	*4.5 mg. INA‡*
70	13/18	0/18	0/15	3/18	4/12	7/12
124	16/18	3/18	2/15	4/18	6/12	9/11
171	14/18				•	
184	16/16	0/18	2/16	3/18	9/12	7/11
700		2/18	3/16	11/16	6/11	

* Lot 1.

** SC treatment: 1.5 mg. on days 1, 33, and 41; animals challenged by intranasal route on day 69.

† SC-INA treatment: 1.5 mg. by each route on days 1 and 34; animals challenged as avove on day 69.

‡ INA treatment: 1.5 mg. on days 1, 33, and 41; animals challenged as above on day 69.

Vaccination with 4.5 mg. of the spherule preparation, administered subcutaneously in 3 doses, afforded protection against challenge doses up to and including 700 arthrospores (TABLE 4). However, after the postchallenge observation period, the animals showed somewhat more extensive lesions at autopsy (TABLE 5) than mice that received 1.6 mg. of the spherule vaccine intramuscularly (TABLE 3). When the immunizing dosage was increased further to a total of 6.0 mg. (administered by the SC and INA routes), lesions were even more extensive in the surviving mice (TABLE 5). The optimal immunizing dosage, regimen, and route have not yet been determined; however, preliminary studies suggest that the intraperitoneal route is less efficacious than the SC route.

It is evident (TABLES 4 and 5) that INA instillation of the spherule vaccine did not increase the immunity of animals also inoculated subcutaneously, as observed by Pappagianis *et al.* (1960) in studies on the immunity induced by infection. However, the lesser immunity induced with spherules administered by the INA route exclusively than by the SC route exclusively (TABLE 4) was in general agreement with the findings of Pappagianis *et al.* (1960), who studied this effect with a viable vaccine of low virulence.

The data in TABLE 6 suggest that the SC injection of a total of 1.5 mg. of the spherule vaccine administered in several doses provides better protection than the same amount of vaccine given in a single dose. There was no mortality over a challenge dosage range of 25 to

TABLE 5

MORTALITY AND SEQUELAE IN IMMUNIZED AND CONTROL MICE SACRIFICED AT 90 DAYS POSTCHALLENGE*

Challenge dose (range)	*Mortality and autopsy findings*	*Control*	*Spherule-vaccinated*			*Mycelium-vaccinated*	
			SC	*SC-INA*	*INA*	*SC-INA*	*INA*
70 to 184	Per cent mortality	86	6	9	19	53	68
	No. survivors autopsied	11	51	42	42	16	7
	Per cent survivors with:						
	No lung lesions	82	47	40	57	44	57
	Minor lung lesions	9	45	31	36	50	36
	Advanced lung lesions	9	8	29	7	6	7
	Liver and/or spleen lesions	0	4	0	0	6	0
	Positive cultures	36	71	79	69	85	55
700	Per cent mortality		11	19	69	55	64
	No. survivors autopsied		16	13	4	5	4
	Per cent survivors with:						
	No lung lesions		38	0	0	40	0
	Minor lung lesions		38	46	70	60	0
	Advanced lung lesions		25	54	0	0	0
	Liver and/or spleen lesions		6	0	0	0	0
	Positive cultures		94	85	0	60	0

*See TABLE 4 for immunization schedule and challenge details.

TABLE 6

IMMUNOGENICITY OF FORMALINIZED SPHERULES OF *COCCIDIOIDES IMMITIS* ADMINISTERED BY DIFFERENT SCHEDULES

Challenge dose (no. arthrospores)	*Dead/total at 90 days postchallenge*		
	Control	*Schedule A*	*Schedule B*
25	5/10		
50	7/10	0/10	0/10
106	8/9	0/10	3/10
195	8/10	0/10	1/10
1350		7/9	7/10

Schedule A: 0.5 mg. administered subcutaneously on days 1, 9, and 18; animals challenged by INA route on day 54.

Schedule B: 1.5 mg. administered subcutaneously in 1 dose on day 18; animals challenged by INA route on day 54.

195 arthrospores in animals treated with 3 doses of vaccine, whereas 10 and 30 per cent of the mice that received a single injection of vaccine died after challenge with 195 and 106 arthrospores, respectively. A challenge dose of 1.4×10^3 arthrospores was lethal to most of the animals treated by either regimen.

The effect of repeated passage in the synthetic-production medium on the immunogenicity of spherules was studied with a second lot of vaccine. The culture was maintained in the spherule or endospore phase by 19 to 20 consecutive passages in BSM-1 over a 4-month period. A preliminary experiment indicates that its immunizing properties (1.6 mg., total in 2 doses, intramuscularly) were considerably less than those of the first vaccine lot, which was a pool obtained from cultures passaged 5 to 8 times. It is presently unknown if this variation is referable to the number of passages or if other factors influence the immunogenicity of different lots.

Discussion

There is compelling epidemiological evidence that active immunity is an important factor in the resistance of man to the more serious manifestations of coccidioidal disease. Almost all newcomers to an endemic coccidioidal area soon acquire dermal sensitivity to coccidioidin (Smith, 1940; 1942), but only a minority develop the symptomatic disease. This suggests that resistance is conferred even by inapparent infections. Furthermore, surveys reported by Smith *et al.* (1957) revealed the absence of second infections among thousands of people who were diagnosed serologically as primary coccidioidal cases. A some-

what similar situation occurs in experimentally infected laboratory animals. The latter, while frequently continuing to harbor the infecting strain for prolonged periods of time, acquire increased resistance to exogenous reinfection (Rixford and Gilchrist, 1896; Smith, 1942, 1951; Negroni *et al.*, 1949; Pappagianis *et al.*, 1959).

The induction of immunity by a nonviable vaccine (Vogel and Conant, 1952) was reported by Vogel *et al.* (1954). These workers showed that the administration of spherules prepared from infected embryonated eggs caused reduced lesions in guinea pigs challenged subsequently by the respiratory route. Friedman and Smith (1956) demonstrated that the administration of killed arthrospores conferred significant resistance to mice challenged by the intraperitoneal route. Pappagianis *et al.* (1960) confirmed the essential findings of Friedman and Smith (1956), but demonstrated further that the immunity measured by intraperitoneal challenge was insufficient to protect many of the mice against comparable challenge doses administered by the INA route.

In the present study, in which the INA route of challenge was employed exclusively, differences in immunogenicity apparently associated with the morphologic phases of *C. immitis* were demonstrated. The spherule-endospore phase of this fungus afforded more protective immunity than vaccines prepared from those phases more commonly observed *in vitro*. However, vaccination with arthrospores or mycelium had protective value. Recently Breslau (1959) discussed similar findings in a comparison of the immunogenicity of killed spherules and mycelium.

A prominent feature among the spherule-immunized mice after challenge (as well as among those immunized with the preparations reported by others) was the presence of continuing infection. Approximately 70 per cent of the spherule-immunized mice yielded positive cultures even 3 to 4 months postchallenge (TABLES 3 and 5). At autopsy, lesions in these animals were not extensive and were generally restricted to the lungs.

Chronic-coccidioidal pulmonary cavitation in the human occurs only in an estimated 2 to 8 per cent of symptomatic cases (Smith *et al.*, 1948). Although this is an important complication of the primary disease, it is rare that dissemination takes place in patients with such cavities (Smith *et al.*, 1948). The prognostically grave progressive or disseminated disease appears, rather, to be an early complication in certain individuals, analagous to progressive primary tuberculosis, and has been termed progressive primary coccidioidomycosis. The rapidity with which dissemination frequently occurs in these individuals suggests a failure of immunity that is presumably developed in the great majority of cases during the early primary phase of the mycosis. Prophylactic immunization, therefore, may be especially desirable in Negroes, Filipinos, or other ethnic groups (Fiese, 1958) that are more prone to develop the disseminated or progressive primary disease.

Summary

The spherule-endospore phase of *Coccidioides immitis* was produced *in vitro* and purified by procedures that removed other morphologic forms of the fungus. After sterilization with formalin, the immunizing properties of this phase were compared in mice to those of purified mycelial and arthrospore vaccines. The protection conferred by administration of the spherule-endospore vaccine was superior to that conferred by the mycelial and arthrospore preparations. After a 90- to 105-day postchallenge observation period, residual lesions in vaccinated survivors contained viable organisms, but the infection appeared to be least extensive in animals that received the spherule-endospore vaccine.

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DIVISION OF ANTHROPOLOGY

SOME CHANGING ROLES OF WOMEN IN SUBURBIA: A SOCIAL ANTHROPOLOGICAL CASE STUDY*

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Social Unrest in the Suburbs

The crabgrass has taken over, the barbecue chimney has an unused look, the aluminum chairs in the backyard are no longer in friendly groups. The stage was set fifteen years ago, but the scenery and its props have changed. In upper-economic level communities the pendulum of time is making its way from contentment-in-the-suburbs to disturbing personal and social unrest. The dream world that envisioned a paradise now sees the realities of daily commuting and the two hours it takes from a man's life, of mortgage payments that never end, of school taxes that increase yearly, of myriad acquaintances and few friends, and of a life increasingly more like that of the city, without urban conveniences.

What changes have these ten years seen? Ten years ago, when suburbia was as far as anyone went and exurbia was for cows, there was a rural feeling to the suburbs. Today suburbia has a studied casualness, a kind of formalized informality. It is an area of living for which a coat was designed just to be worn in a car, with the car pool, not the sports car, in mind.

If there was one lure ten years ago, it was the glory of suburban schools. These schools may still be glorious, but higher taxes have tarnished that glory. Moreover, "We'd better send the boy away to boarding school" is part of every dinner conversation, and each year boys enter at an earlier level.

The ease of homogeneity, of like seeking like – so attractive ten years ago – is proving dull. Says one suburban matron: "When we moved here, I loved the idea that there were so many of 'our kind' to choose from – college graduates, successes in their fields. Now I can't stand the sameness of the thinking and that same every-Saturday-night party with its little black dresses, each with a pin at the corner of its low-cut neck."

What Webster defines as the intellectual content of civilization and the Romans called *humanitas*, we give the less happy phrase of "culture." If culture flowers in the city, it withers in the suburbs despite intensive and anxious nurturing. Schools for adults flourish throughout the suburbs, but ten years' experience has shown that courses that give homework

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do not attract students, so that the so-called intellectual courses become lectures, and the sell-out courses are bridge, golf, and woodworking. Women take a variety of day courses, with little genuine intellectual content. Dilettantism thrives in suburbia.

Ten years have pointed up the inconvenient mechanics of travel. There is no such thing as gently exposing children to cultural experiences; the exposure always proves negative. Says one mother: "Children see less these days, and are less independent than when I was a city child. They can't go anywhere by themselves. Chauffeuring is as bad for them as for me."

While sports have continued to thrive, although now with greater intensity, there have been changes in these ten years. Factories have golf teams, and golf clubs have bowling teams.

Suburban politics is feeling a change. Conservatism and Republican majorities, a traditional characteristic of suburbia, still hold, but the grip is not so sure. Civic organizations, of course, are still controlled by an inner group. Says one resident: "I pay money to the Friends of the Library, to the Friends of Animals, but the only ones who run them are the Friends of Friends."

Robert Wood,[1] in a recent volume titled *Suburbia*, notes that suburbanites are concerned in an especially intense way about local affairs: zoning, street paving, and garbage collection. One resident, agreeing with him, declares: "What this town needs is people to stay home from meetings." However, paradoxically, another resident seems to feel that community earnestness has decreased, giving credit, in part, to early heart attacks.

There is more privacy. No man is an island, but the bridge over the moat can frequently be raised. This private security has given public courage. Ten years ago, the PTA was off-limits for criticism. Today people are wondering about PTAs, and are wondering aloud. It may even be that conformity is on the wane. However, as one suburban commuter notes: "How nonconformist can you be when you must make the 8:26?" That is one aspect that has not changed: the tightness of time.

Changes in the Life of Women

Living conditions in the suburbs and the place of suburbia in life in the United States are in flux for suburban residents. For women, there are even added complexities.

Married women have been going back to work at a greater rate than ever before. Since 1950, says the National Manpower Council,[2] the largest source of new workers in the labor force has been women in their middle and later years. This trend changes the climate of opinion for the return to work of women of all economic levels.

Women continue to be haunted by their education. Margaret Mead[3] reports "We have the striking paradox of women who are educated like

men and who can do most of the things men do but who still are taught to prefer marriage to any other way of life ... In this paradox lies much of the confusion for women today."

In addition, for women who moved to the suburbs ten years ago, a new level of life is beginning. Now, for the first time, they can see a future where the family plays a diminishing role. At the same time, society encourages them to cut apron strings once that family is grown.

Questions and Speculation

Has woman's response to the changing mores brought changes in her pattern of thinking? If we can judge from one survey's results, she is disquieted. A survey questionnaire was mailed to two hundred women, and elicited a response of more than fifty per cent. This fact alone may have as much significance as the validity and value of the questionnaire itself.

How will this disquiet resolve itself? In work for gain? In volunteer work with a purpose or volunteer work that is frenzied activity? In taking courses with the objective of professionalism or self-fulfillment, or both? In too many courses, none in depth?

Women's middle years cause speculation and conflict among many authorities. Theodore Caplow,[4] a sociologist, feels that while the housewife in her middle years may have no personal economic need, she has the psychological need to justify herself, for our culture emphasizes striving and economic productivity. The Department of Labor in its *1958 Handbook on Women Workers*[5] suggests that "very few women are working just for the satisfaction of having a job." David Riesman[6] sees women "... being driven out of many of the areas in which they formerly occupied their leisure with amateur competence."

Guides to a Survey

With these statements in mind, a questionnaire was mailed to more than 200 women of an upper-economic group (annual income over $25,000), college-educated, ranging in age from 25 to 35, living in the suburbs with children and husband.

A high-income community was used to minimize economic need; the age range of 25 to 35 would offer a cross section of residents who are feeling the impact of change.

Study hypotheses. In this limited survey, which represented an attempt to formulate, define, and explain the problems faced by married women living in a suburban community, it was postulated that: (1) married women will be more likely to work if they have worked before; and (2) they will be more likely to work if their mothers have worked for gain or if their mothers have been very active volunteers (very active is defined as devotion of two to three days per week).

Some alternative postulates were stated as study hypotheses: (1) women who major in certain fields will need less vocational guidance than others; (2) women who have once worked will need less guidance than those who have not; and (3) whether these women will educate themselves further in order to return to work is another area to be explored.

Survey findings. Seventy-seven responses were used, including those of 13 women who were personally interviewed. Total mail response was 107, but some arrived too late or were from those over the 35 age limit and therefore were not used.

Ages ranged between 25 and 35. Most women had 2 children. One third had married at 20 and under, more than half between 21 and 23. Their husbands were in the high-economic position, professional men comprising the majority. All women had had some college education, only one had a graduate degree. Seventy-eight per cent had had B grades in college.

Their majors were the customarily popular ones: arts, social science, and education. Whereas education as a major choice runs 46 per cent on a national basis, it ran 12 per cent for this group.

Two thirds of these women had worked before marriage. More than half had worked full time: one third under 2 years, one third 2 years, and one third more than 2 years.

Sixty per cent continued to work after marriage, 35 per cent worked full time, 25 per cent part time. After children arrived, the full-time figure dwindled perceptibly to 4 per cent; the part-time figure remained at 25 per cent. Fifty-three per cent enjoyed what they did; of these, 36 per cent would go back, 56 per cent would not, and 8 per cent did not know.

Currently, 62 per cent of these women are doing volunteer work, largely of the one-day and under variety. Forty-five per cent take courses, most for self-improvement only; very few are working toward a degree.

Forty-four per cent of the mothers of these women have worked; of these 18 per cent are now working part time and 9 per cent full time. Eighty-four per cent have done volunteer work, of whom 54 per cent were very active.

Up to this point, the questionnaire asked factual information within the framework of reality. It is in the area of future plans and hopes that we see attitude rather than action. We have no way of knowing whether in five years these plans will be fact or fantasy.

The gap between yearning and doing is wide. An alumnae association sponsored a two-session forum in the suburbs on "How Women in the Middle Years Can Return to Work." Twenty-five women attended. As a beginning step, each woman was asked to come to the second meeting with a résumé. A soul-searching step, it took thought and sincerity of purpose. Only one woman came prepared to the next meeting.

Eli Ginzberg[7] of Columbia University believes that fantasy plays

a large part in occupational choice and that women, searching for something intangible, fall prey to it. Witness the small businesses that open and close with sad regularity, as one woman's husband reminds her that he likes her to come along on business trips; another woman forgets until spring the beauties of golf, and then who will tend the antiques shop? If a woman does not view her career from the perspective of her own and her family's needs and desires, she is unthinking and unrealistic.

However, there is another side to the coin, and it is in the approach of one woman who declares: "If you have the desire and the drive, you can accomplish what you want to do."

We, too, must be realistic. We must view the following statistics as measures of unrest and not always of reality, for our problem is compounded further by those women who answer as they think they should.

More than half of these women plan to go to work: 13 per cent immediately, the rest in 5 to 15 years. Sixteen per cent do not know their plans; 32 per cent know they will never work.

Of those expecting to go to work, 75 per cent feel they are inadequately prepared, and of these, more than 80 per cent plan to go to school; some are there now. Many plan to change from original major fields, especially in the arts and social science fields. One social science major says: "I have always felt that graduating from college with a degree such as mine prepared me for no special kind of work."

These women will change their fields if they find no vocational outlet; they will change their fields if a change of interest has taken place over the years, as evidenced by one comment: "Although I enjoyed the world of fashion as a younger person, I find that it has no interest for me now as far as careers go. I want to be in a field that will help the world, if only a little."

No one who majored in education planned to change her field.

For those women who will not work for gain, there will be volunteer work, perhaps expressing this woman's theory: "A married woman's chief objective is to make a good home for both her husband and her children. If and when she is able, some time should be devoted to volunteer work." More than 25 per cent of women who will work will also do volunteer work.

More than half of those questioned would have liked vocational guidance, or better guidance, in college. "Yes," with five underlines, says one woman. "If I had had proper guidance in college I feel that I would have gone on for my M.A. and would be able to teach if I wanted to." At least one half of these women would like vocational guidance now, to learn of vocational opportunities and to evaluate their capacities.

Interpretation and Generalizations

That women will be more likely to work if they have worked before. Of the women who had once worked, 72 per cent plan to work again; a small

percentage of the women who had never worked before now want to do so. (If women "... have never worked," says Alice Gore King, Executive Director of Alumnae Advisory Center, a nonprofit placement agency in New York, N.Y., "they find it more difficult than it need be to start to work after the children are grown.")

That women who major in certain fields will need less vocational guidance than others. Arts and social science majors asked for more guidance than education, psychology, and business majors.

Some relationships we expected to find: that women will be more likely to work if their mothers have worked for gain or if their mothers have been very active volunteers.

One of the hypotheses was not supported by the data. There was no relationship established between those who had worked needing less guidance than those who had never worked. Guidance in college was for them, a stopgap while seeking a husband. Thus guidance today must follow different directions, based upon a more thoughtful and realistic approach.

A large proportion of these women felt inadequately prepared for their career and, of these, most plan to go back to school.

What other inferences might be drawn from these data? We can attach great significance to the large response to the study, suggesting that this is a subject of intense interest. Women, even younger ones, are concerned about what they are going to do with themselves when their children are grown. The future looms large now.

It is significant that 50 per cent of these women, from an upper-economic group, see themselves in remunerative work. In other generations, these were the women who carried the brunt of charitable work. Charity depended on them, and they themselves felt a moral obligation. This moral obligation now has apparently disappeared, replaced by the psychological need to be economically productive.

In making their choice, women are reflecting the social attitudes of our time: (1) we are an economic society, and all things are valued in terms of money; and (2) women, educated as men are educated, have been given the same objectives.

The liberal arts colleges, which used to specialize in the humanities and whose objective was the educated person, have tended to become vocationally oriented. The courses that flourish are those that are economically geared, while philosophy and the classics languish. Given a man-sized education, women begin to feel that the only proper use of it, in this dollar-conscious economy, is a paid job.

Conclusions

It is clear that the traditional volunteer activities of women are no longer of interest to them. Women desire to be paid for what they do, because they want the social status that money brings. This supports

Mirra Komarovsky's[8] statement that "... generally low status is accorded unpaid hobbies and volunteer activities ... being important in our society is being professional, not a dilettante." For this group, the ability to earn money is a way of distinguishing oneself. There are exceptions: some unpaid jobs have more status than paid ones. A state board position with the League of Women Voters has more prestige than a doctor's assistant.

To find the paid career that will fit in with all angles of married life is not easy. Part-time work is often the answer, but the part-time work available in the suburbs is low-level. "Sales representative for encyclopedia; woman to sell fashion by phone" – the fact that women take these jobs shows the low rating given volunteer work.

Has the volunteer field itself helped to create this attitude? Has the field become so professionalized that there is no room for the woman of education, perception, and responsibility, except in minor roles? Today's woman would do as her rich grandmother did, but she would do it differently, because she is better educated. Given the proper societal mores, she would do it willingly. Today it is not unusual to ask a married woman what she does. For many, volunteer work does not suffice as an answer.

The woman in the suburbs, looking for a career, paid or volunteer, meets many obstacles. If she wants a career in volunteer activities, she discovers it often reaches a dead end in fund-raising. If she wants to go to school to retrain, she is limited, in point of time, in the schools she can attend. If she wants a paid job, she finds few jobs that use her talent.

To all of these plaints, the city has the readier answers. It offers more volunteer opportunities with status; it offers, on a subway ride, numerous graduate schools; it offers more part-time jobs, the beginning step to full-time work. Interestingly, the editors of *Fortune*,[9] in their *Exploding Metropolis*, note a "small but significant" move back to the city. Is the desire of women to go to work a causative factor in this shift?

When families moved to the suburbs ten years ago, they were looking for a good way to live life, for a place where child raising would be simplified and expenses minimized, and where small-town life, in its happier aspects, would be realized. If father is to spend two hours a day commuting, let it be counterbalanced by an idyllic existence for mother and the children. However, the equation is not equating. Taxes have skyrocketed; child raising has not been simplified, but rather has become more complex than in the city. Mother is bored and counteracts lonesomeness with too much belongingness. She, who sought freedom in the move to the suburbs, finds more demands on her time and, with it, more responsibility.

How will she carve out her future? Will she "sink back into indif-

ference''[6] or, striking out in all directions, hope to stumble on one right way? Or will she find a sensible solution, unique to her? To accomplish the latter, she must be firm of purpose, for society, as it now stands, offers little help. For society to help, it must alter the framework built around and into the situation. Given proper status, volunteer work could be an answer; given proper cultural outlets, many women would not feel the need for a job; given an understanding society, more and better part-time jobs could be made available.

Women are shifting gears in making this uphill climb, as they try to find the way for themselves in terms of their family responsibilities and in terms of society. The grinding noise of a shift that is uneven is what can be called unrest among women in suburbia.

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DIVISION OF OCEANOGRAPHY AND METEOROLOGY

METEOROLOGY: A REDISCOVERED SCIENTIFIC FRONTIER*

Thomas F. Malone†

The Travelers Insurance Company, Hartford, Conn.

Early in 1958, the president of the National Academy of Sciences, Washington, D. C.[1] remarked that "... an exciting opportunity for major progress in meteorological science exists at the present time .... We are potentially on the threshold of a new era in understanding our environment." This thoughtful comment by a respected spokesman for the scientific community is indicative of a growing interest in, and appreciation for, the scientific problems of the atmosphere. The fact that meteorology is concerned with the scientific problems of the atmosphere has become somewhat obscured during the past century because of the close identification of the word "meteorology" with the application of meteorological knowledge to the practical problem of weather forecasting.

To view with proper perspective what is happening today, it is helpful to note that progress toward an understanding of our atmospheric environment has taken place somewhat unevenly over the past twenty-five hundred years. Four significant turning points can be identified. A breakthrough of a sort was achieved by the perspicacious Greeks, who lifted study of the atmosphere out of the context of mythology, in which weather was ascribed to the whims of a host of deities, and placed it on a level characterized by a scientific attitude of reason and a physical interpretation of systematic observations. About 350 B.C., Aristotle was able to summarize all existing knowledge in his *Meteorologica*, a compendium that remained the authoritative reference work in this field for nearly two thousand years.

A second significant advance occurred with the invention of the thermometer, the barometer, and the hygrometer during the Sixteenth and Seventeenth centuries. This opened the first quantitative era in meteorology: a period when discrete measurements were analyzed carefully to gain a better understanding of the laws of nature. The researches of many great scientists were concerned directly or indirectly with atmospheric problems. Galileo, Evangelista Toricelli, Blaise Pascal, Robert Boyle, Jacques A. Cesar Charles, Rene Descartes, Isaac Newton, Anders Celsius, Benjamin Franklin, Joseph Black, Joseph Louis LaGrange, Pierre Simon de Laplace, John Dalton and many others left their foot-

* This paper, illustrated with slides, was presented at a meeting of the Division on March 29, 1960.

† President, The American Meteorological Society, New York, N.Y.

prints in meteorology as they became intrigued with the explanation of physical phenomena in the atmosphere.

The next major development took place during the Nineteenth Century when Brandes, in 1820, prepared the first weather map in an attempt to portray an integrated picture of the atmosphere on a synoptic basis. The effort was premature, but it did provide a basis for the preoccupation during the latter half of the Nineteenth Century with the task of depicting successive states of the atmosphere with the objective of preparing weather forecasts. In one sense, the emphasis on weather prediction detracted from concentration on the problem of understanding, with the result that scientific progress was rather slow during the first part of the Twentieth Century. In a broader sense, however, this was a necessary and even desirable step in the scientific advance of meteorology because the economic importance of even admittedly unsatisfactory weather forecasts made possible the national and international networks of observing stations required to view the atmosphere in its global dimension. From these data and from fragmentary and scattered studies on the fundamental physics of atmospheric processes, there has begun to emerge during the past two or three decades a reasonably coherent picture of the scientific problem to be solved in the lower portion of the atmosphere. The fact that elements of the problem can even be formulated is perhaps the most exciting development in meteorology over the past three thousand years.

There are several reasons for believing that progress in solving these problems, now that they are formulated, can be expected to proceed rapidly during the next two decades:

First, there is a growing realization that the atmosphere is one of our great natural resources that needs serious development and exploitation.

Second, the simple fact that the scientific community at large has come to appreciate the facts that basic research on atmospheric problems is exciting and challenging and that it presents many opportunities for immediately extending the frontiers of our knowledge is already beginning to attract into atmospheric research the kind of scientific competence needed to augment our slim manpower resources.

Third, the development of new research tools such as high-level radiosondes, radar, sensing devices that can be mounted on airborne platforms, isotope-tracing techniques, high-speed electronic computers, and meteorological satellites is creating opportunities to subject the atmosphere to a detailed scientific scrutiny.

Fourth, the economic pressure for weather predictions of greater accuracy and further extension into the future will help to provide support for the fundamental research effort to augment our basic understanding of the atmosphere and why it behaves as it does.

Finally, the initiative of thirteen of our great universities and of the National Science Foundation, Washington, D.C., in joining forces to

establish the University Center for Atmospheric Research[2] augurs well for laying the foundation for a coordinated research program combining the essential ingredients of a broad interdisciplinary intellectual effort and the array of large and complicated facilities required to mount a research effort on a scale commensurate with the magnitude of the problem.

From the research program now in the process of being strengthened at the universities and in private and government laboratories and about to be inaugurated at the University Center for Atmospheric Research, it is possible to venture a few personal opinions concerning developments of some significance. Among other developments, these are probable:

(1) The point of view will prevail that the earth's atmosphere is but one special case of planetary atmospheres in general and that we are just as likely to learn things about our atmosphere from the study of the atmospheres of other planets as the biologist is apt to learn about the characteristics of a particular genus by studying other genera.

(2) The development of a statistical mechanics of the atmosphere will modify the classic Newtonian approach to hydrodynamics and bring the theoretical treatment of air motion into harmony with the measurement framework within which successive states of the atmosphere are observed.

(3) A thermodynamics of open systems capable of dealing realistically with the thermally active hydrodynamic system that typifies the atmosphere will be developed.

(4) Greatly increased attention will be given to the exchange processes of the ocean-atmosphere interface. With the expansion in oceanographic research during the next decade, it is essential that the closest ties be established between oceanography and meteorology. Synoptic array of oceanographic observations will aid this work materially.

(5) Greatly increased attention will be devoted to the scientific problems concerned with the structure, composition, diffusion, photochemistry ionization, dynamics, and magnetohydrohynamics of the upper atmosphere. Here, too, discrete measurements will soon be replaced by observational networks.

(6) Greatly increased attention will be given also to the neglected problem of physiological response of human beings to our atmospheric environment and its changes.

With somewhat greater temerity, one may predict that by 1980 we shall have reasonably good answers to the following questions, which are fundamental or practical, or both: (1) What are the details of the manner by which the earth-atmosphere-ocean system communicates energy with the sun and the other elements of the universe? (2) How does the atmosphere make rain? (3) How is lightning produced? (4) How are tornadoes and hurricanes formed? (5) Is climate control feasible?

The economic justification for support of basic atmospheric research is that, over the long term, it will provide ultimately the knowledge that

will permit us either to control the weather or to predict it. It is barely possible, but rather unlikely, that we can do both.

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CONFERENCES HELD

SECTION OF BIOLOGICAL AND MEDICAL SCIENCES

SECOND CONFERENCE ON THE MECHANISMS OF CELL DIVISION

Thursday, March 3 and
Friday, March 4, 1960

Conference Co-Chairmen:
Paul R. Gross, New York University
New York, N. Y.
and
Daniel Mazia, University of California
Berkeley, Calif.

THURSDAY, MARCH 3, 1960

Session Chairman: M. J. Kopac
New York University
New York, N. Y.

9:00 A.M. –
Greetings from the Academy – Robert L. Kroc, Chairman, Section of Biological and Medical Sciences, The New York Academy of Sciences, New York, N. Y.; Warner-Lambert Research Institute, Morris Plains, N. J.

Introductory Remarks – Paul R. Gross, New York University, New York, N. Y.

"Fine Structure of Small Parts of Chromosomes After Localized Ultraviolet Irradiation" – William Bloom, University of Chicago, Chicago, Ill.

"Aster-Associated Particles in Cleavage" – L. I. Rebhun, Princeton University, Princeton, N. J.

"On the Physical Nature of the Mitotic Spindle" – S. Inoué, Dartmouth Medical School, Hanover, N. H.

"Fine-Structure of Spindle Components" – K. R. Porter, The Rockefeller Institute, New York, N. Y.

"Experimental and Comparative Studies on the Chromosome Movements" – G. Östergren, University of Lund, Lund, Sweden.

"Autoradiographic Studies of Chromosome Duplication and Related Events" – J. H. Taylor, Columbia University, New York, N. Y.

Session Chairman: Daniel Mazia
University of California
Berkeley, Calif.

2:00 P.M. –

"Dynamic Aspects of Mitotic Apparatus Protein" – H. A. Went, State College of Washington, Pullman, Wash.

"Formation of the Spindle in Amphibian and Mammalian Cells" – E. W. Taylor, University of Chicago, Chicago, Ill.

"Disappearance of Spindles and Other Birefringent Mitotic Structures After Microbeam Irradiation of Cytoplasm" – R. E. Zirkle, R. B. Uretz, and R. J. Haynes, University of Chicago, Chicago, Ill.

"Deoxyribosides in Relation to the Mitotic Cycle" – H. Stern, Department of Agriculture, Ottawa, Ont., Canada.

6:30 P.M. –

"The Chemistry of Mitosis" – Daniel Mazia, University of California, Berkeley, Calif.

FRIDAY, MARCH 4, 1960

Session Chairman: G. Oster
Brooklyn Polytechnic Institute
Brooklyn, N. Y.

9:00 A.M. –

"Electrophoretic Studies on Protoplasm During Mitosis" – Walter L. Wilson, University of Vermont College of Medicine, Burlington, Vt.

"Furrow Induction in Sea Urchin Eggs" – D. Marsland and A. Zimmerman, New York University, New York, N. Y.

"Macromolecular Interactions Underlying Cell Division" – N. G. Anderson, Oak Ridge National Laboratory, Oak Ridge, Tenn.

"Heavy Water Inhibition of Cell Division: An Approach to Mechanism" – Paul R. Gross, New York University, New York, N. Y., and W. Spindel, Rutgers University, Newark, N. J.

"Contractile Proteins and Mitosis" – T. Hayashi, Columbia University, New York, N. Y.

Session Chairman: M. L. Petermann
Sloan-Kettering Institute
New York, N. Y.

2:00 P.M. –

"The Nucleocytoplasmic Ratio and Cell Division" – H. I. Hirschfield, New York University, New York, N. Y.

"Effects of Hormones on Mitosis in Mouse Ear Epidermis, *in Vitro*" – S. Gelfant, Syracuse University, Syracuse, N. Y.

"Controlled Division Synchrony and Growth in Microorganisms" – T. W. James, University of California at Los Angeles, Los Angeles, Calif.

"Comparative Aspects of Phosphate Metabolism in Normal and Synchronously Dividing Cells" – O. Scherbaum, University of California at Los Angeles, Los Angeles, Calif.

"Cell Population Kinetics" – H. Quastler, Brookhaven National Laboratory, Upton, L. I., N. Y.

"Environmental Feedback Control of Cell Division" – A. D. Glinos, Walter Reed Army Institute of Research, Washington, D. C.

"Regulation of the Mitotic Rate in Mammalian Organs in Normal and Pathological Conditions" – H. F. Stich, University of Saskatchewan, Saskatoon, Sask., Canada.

Robert L. Kroc
Chairman

Charles Noback
Vice-Chairman

SECTION OF GEOLOGICAL SCIENCES

AND SECTION OF CHEMICAL SCIENCES

GEOCHRONOLOGY OF ROCK SYSTEMS

Thursday, March 3
Friday, March 4 and
Saturday, March 5, 1960

Conference Chairman: J. Laurence Kulp
Lamont Geological Observatory, Columbia University
Palisades, N. Y.

THURSDAY, MARCH 3, 1960

METHODOLOGY

Session Chairman: G. J. Wasserburg
California Institute of Technology
Pasadena, Calif.

9:00 A.M. –
Greetings from the Academy – Rhodes W. Fairbridge, Chairman, Section of Geology, The New York Academy of Sciences, New York, N. Y.

Introductory Remarks – J. Laurence Kulp, Lamont Geological Observatory, Columbia University, Palisades, N. Y.

"Present Status of the Decay Constants" – L. E. Glendenin, Argonne National Laboratory, Lemont, Ill.

"Isotopic Abundances in Common Strontium" – P. W. Gast, University of Minnesota, Minneapolis, Minn.

"Diffusion of Argon in Potassium Minerals" –
(1) J. F. Evernden, University of California, Berkeley, Calif.
(2) S. B. Brandt, Academy of Sciences of the U.S.S.R., Moscow, U.S.S.R.
(3) E. K. Gerling, Laboratory for Precambrian Geology, Leningrad, U.S.S.R.

"The Problem of Potassium Analysis" – W. R. Pinson, Massachusetts Institute of Technology, Cambridge, Mass.

"Geochemical Alteration" –

(1) S. R. Hart, Massachusetts Institute of Technology, Cambridge, Mass.
(2) L. T. Silver, California Institute of Technology, Pasadena, Calif.
(3) G. R. Tilton, Carnegie Institution of Washington, Washington, D.C.
(4) K. K. Zhirov, State University, Moscow, U.S.S.R.

DATING SEDIMENTARY ROCKS

Session Chairman: G. W. Wetherill
Carnegie Institution of Washington
Washington, D. C.

2:00 P.M. –

"Volcanic Rocks" –

(1) R. E. Folinsbee, University of Alberta, Edmonton, Alta., Canada.
(2) G. H. Curtis, University of California, Berkeley, Calif.

"Glauconite" –

(1) N. I. Polevaya, All Union Institute of Geology, Leningrad, U.S.S.R.
(2) P. M. Hurley, Massachusetts Institute of Technology, Cambridge, Mass.

"Sylvite" – N. I. Polevaya, All Union Institute of Geology, Leningrad, U.S.S.R.

"Black Shale" – J. C. Cobb, Brookhaven National Laboratory, Upton, N. Y.

"Detrital Rocks" – A. E. Krilov, All Union Institute of Geology, Leningrad, U.S.S.R.

Speaker: A. O. C. Nier
University of Minnesota
Minneapolis, Minn.

FRIDAY, MARCH 4, 1960

THE POSTCRYPTOZOIC GEOLOGICAL TIME SCALE

Session Chairman: J. Laurence Kulp
Lamont Geological Observatory, Columbia University
Palisades, N. Y.

9:00 A.M. –

"Critical Points in North America" –

(1) J. A. S. Adams, The Rice Institute, Houston, Texas or,
J. J. W. Rogers, The Rice Institute, Houston, Texas.
(2) G. H. Curtis, University of California, Berkeley, Calif.
(3) H. Faul, United States Geological Survey, Washington, D. C. and
W. H. Pinson, Massachusetts Institute of Technology, Cambridge, Mass.

"Critical Points in Europe" –
(1) R. St. J. Lambert, Oxford University, Oxford, England.
(2) H. Faul, United States Geological Survey, Washington, D. C.

"Critical Points in Asia and Other Continents" – M. M. Rubinshtein, Georgian Institute of the Academy of Sciences, Tbilisi, Georgian SSR, U.S.S.R.

Discussion of Geological Time Scale

THE AGE OF THE BASEMENT ROCKS OF THE WORLD
PART ONE: NORTH AMERICA

Session Chairman: J. T. Wilson
University of Toronto
Toronto, Ont., Canada

2:00 P.M. –
"Grenville and Appalachian Provinces" –
(1) F. D. Eckelmann, Brown University, Providence, R. I.
(2) P. M. Hurley, Massachusetts Institute of Technology, Cambridge, Mass.
(3) L. E. Long, Lamont Geological Observatory, Columbia University, Palisades, N. Y.
(4) G. R. Tilton, Carnegie Institution of Washington, Washington, D.C.

"Canadian Shield" –
(1) L. T. Aldrich, Carnegie Institution of Washington, Washington, D.C.
(2) M. N. Bass, Carnegie Institution of Washington, Washington, D.C.
(3) H. W. Fairbairn, Massachusetts Institute of Technology, Cambridge, Mass.
(4) S. S. Goldich, United States Geological Survey, Washington, D.C.
(5) G. W. Wetherill, Carnegie Institution of Washington, Washington, D. C.
(6) C. H. Stockwell, Geological Survey of Canada, Ottawa, Ont., Canada and,
R. K. Wanless, Geological Survey of Canada, Ottawa, Ont., Canada.

"Rocky Mt. Province" –
(1) P. E. Damon, University of Arizona, Tucson, Ariz.
(2) P. W. Gast, University of Minnesota, Minneapolis, Minn.
(3) J. Lipson, University of Alberta, Edmonton, Alta., Canada.

Other Areas

SATURDAY, MARCH 5, 1960

THE AGE OF THE BASEMENT ROCKS OF THE WORLD
PART TWO: EURASIA

Session Chairman: A. I. Tugarinov
Vernadsky Institute of Geochemistry
Academy of Sciences of the U.S.S.R.
Moscow, U.S.S.R.

9:00 A.M. –
"U.S.S.R." –
(1) A. P. Vinogradov, Vernadsky Institute of Geochemistry, Academy of Sciences of the U.S.S.R., Moscow, U.S.S.R. or,
A. I. Tugarinov, Vernadsky Institute of Geochemistry, Academy of Sciences of the U.S.S.R., Moscow, U.S.S.R.
(2) L. V. Komlev, V. G. Khlopin Institute, Leningrad, U.S.S.R.

"Fennoscandia" –
(1) O. Kouvo, Outokumpu Company, Outokumpu, Finland.
(2) J. Laurence Kulp, Lamont Geological Observatory, Columbia University, Palisades, N. Y.
(3) A. A. Polkanov, Laboratory for Precambrian Geology, Leningrad, U.S.S.R.

"British Isles" – B. J. Giletti, Oxford University, Oxford, England.

THE AGE OF THE BASEMENT ROCKS OF THE WORLD
PART THREE: AFRICA AND AUSTRALIA

Session Chairman: R. D. Russell
University of British Columbia
Vancouver, B.C., Canada

11:00 A.M. –
"Australia" –
(1) P. M. Jeffery, The University of Western Australia, Nedlands, Australia.

(2) H. W. Fairbairn, Massachusetts Institute of Technology, Cambridge, Mass.

"Africa" –

(1) L. O. Nicolaysen, Bernard Price Institute of Geophysical Research, University of the Witwatersrand, Milner Park, Johannesburg, Union of South Africa.

(2) L. Cahen, Musée Royal du Congo Belge, Tervueren, Belgium.

THE AGE OF THE BASEMENT ROCKS OF THE WORLD
PART FOUR: OTHER AREAS

Session Chairman: M. Kay
Columbia University
New York, N. Y.

2:00 P.M. –

"Central and South America" –

(1) P. M. Hurley, Massachusetts Institute of Technology, Cambridge, Mass.

(2) W. H. Pinson, Massachusetts Institute of Technology, Cambridge, Mass.

"Oceania and Antarctica" – A. E. Krilov, All Union Institute of Geology, Leningrad, U.S.S.R.

SYNTHESIS OF CRUSTAL HISTORY AND PRECAMBRIAN TIME SCALE

Session Chairman: P. M. Hurley
Massachusetts Institute of Technology
Cambridge, Mass.

3:00 P.M. - 5:00 P.M. –

(1) J. T. Wilson, University of Toronto, Ont., Canada.

(2) G. J. Wasserburg, California Institute of Technology, Pasadena, Calif.

(3) A. A. Polkanov, Laboratory for Precambrian Geology, Leningrad, U.S.S.R.

SECTION OF BIOLOGICAL AND MEDICAL SCIENCES

ASPECTS OF INSECT ENDOCRINOLOGY

Friday, March 18, 1960

Conference Co-Chairmen

Dietrich Bodenstein, University of Virginia, Charlottesville, Va.
Karl Maramorosch, The Rockefeller Institute, New York, N.Y.

FRIDAY, MARCH 18, 1960

Session Chairman: Dietrich Bodenstein
University of Virginia, Charlottesville, Va.

9:00 A.M.-

Greetings from the Academy - Robert L. Kroc, Chairman, Section of Biological and Medical Sciences, The New York Academy of Sciences, New York, N. Y.; Warner-Lambert Research Institute, Morris Plains, N.J.

Introductory Remarks - Dietrich Bodenstein, University of Virginia, Charlottesville, Va.

"Blood Proteins in Insect Development" - Hans Laufer, Johns Hopkins University, Baltimore, Md.

"Hormonal Control of Egg Maturation in Insects" - Franz Engelmann, Albert Einstein College of Medicine, Yeshiva University, New York, N.Y.

"Oxidative Enzymes and the Injury Metabolism of Diapausing Silkworms" - David G. Shappirio, University of Michigan, Ann Arbor, Mich.

"Hormonal Control of Cast Differentiation in Termites" - Martin Luscher, Zoological Institute, University of Bern, Bern, Switzerland.

Session Chairman: Berta Scharrer
Albert Einstein College of Medicine, Yeshiva University,
New York, N.Y.

2:00 P.M.-

"Hormonal Control of Scale Development and Molting Behavior in Insects" - Hans Piepho, University of Göttingen, Göttingen, Germany.

"The Effects of Insect Hormones on Their Parasites" - L. R. Cleveland, Harvard University, Cambridge, Mass., and University of Georgia, Athens, Ga.

"Present Status of Insect Tissue Culture" - Richard C. Sanborn, Purdue University, Lafayette, Ind.

Robert L. Kroc
Chairman

Charles Noback
Vice-Chairman

CARDIOVASCULAR EFFECTS OF NICOTINE AND SMOKING

Thursday, March 24
Friday, March 25, and
Saturday, March 26, 1960

Conference Chairman: Carl J. Wiggers
Frank E. Bunts Educational Institute
Cleveland, Ohio

Organizing Chairman: McKeen Cattell
Cornell University Medical College
New York, N. Y.

THURSDAY, MARCH 24, 1960

THE ABSORPTION AND FATE OF NICOTINE

Session Chairman: Harvey B. Haag
Medical College of Virginia
Richmond, Va.

9:00 A.M. –
Greetings from the Academy – Charles Noback, Vice Chairman, Section of Biological and Medical Sciences, The New York Academy of Sciences, New York, N. Y.

Introductory Remarks – Carl J. Wiggers, Frank E. Bunts Educational Institute, Cleveland, Ohio.

"Nicotine and Its Botanical Sources" – R. F. Dawson and Marie L. Solt, Columbia University, New York, N. Y., and David R. Christman, Brookhaven, N. Y.

"The Absorption of Nicotine from Various Sites" – Janet Travell, Cornell University Medical College, New York, N. Y.

"Absorption of Nicotine Under Various Conditions of Tobacco Use" – Paul S. Larson, Medical College of Virginia, Richmond, Va.

"The Excretion and Metabolism of Nicotine" – Herbert McKennis, Medical College of Virginia, Richmond, Va.

PHARMACOLOGICAL ACTIONS OF NICOTINE AND TOBACCO SMOKE

Session Chairman: Charles J. Kensler
Boston University School of Medicine
Boston, Mass.

2:00 P.M. –

"Components of Pharmacological Interest in Tobacco Smoke" – Charles J. Kensler, Boston University School of Medicine, Boston, Mass.

"The Pharmacological Actions of Nicotine" – Julius H. Comroe, Jr., University of California Medical Center, San Francisco, Calif.

"Mechanism of Action of Nicotine in Impairing Impulse Transmission in Autonomic Ganglia" – Edward W. Pelikan, Boston University School of Medicine, Boston, Mass.

"The Action of Nicotine on the Heart" – J. Harold Burn, Oxford University, Oxford, England.

"The Effect of Nicotine and Smoking on the Secretion of Epinephrine" – – Daniel T. Watts, West Virginia University Medical Center, Morgantown, W. Va.

FRIDAY, MARCH 25, 1960

THE INFLUENCE OF NICOTINE AND SMOKING ON THE PERIPHERAL CIRCULATION

Session Chairman: J. Harold Burn
Oxford University
Oxford, England

9:00 A.M. –

"The Action of Nicotine on the Blood Vessels" – J. Harold Burn, Oxford University, Oxford, England.

"Comparison of the Results Obtained by Various Methods for the Measurement of the Peripheral Circulation Before and After Smoking" – Jack Freund, Medical College of Virginia, Richmond, Va.

"Influence of Nicotine on the Blood Flow of the Skin and Muscles in Normal Subjects" – Hans Rottenstein, George Peirce, Ellier Russ, David Felder, and Hugh Montgomery, University of Pennsylvania, School of Medicine, Philadelphia, Pa.

"Effect of Smoking on the Peripheral Circulation in Relation to the Environmental Temperatures" – J. Edwin Wood, Medical College of Georgia, Augusta, Ga.

"The Acute Effects of Chewing Tobacco and Smoking in Habitual Users" – David L. Simon, University of Cincinnati College of Medicine, Cincinnati, Ohio.

"Responses of the Peripheral Veins in Man to the Intravenous Administration of Nicotine" – John W. Eckstein and A. W. Horsley, State University of Iowa College of Medicine, Iowa City, Iowa.

"Tobacco Hypersensitivity: I. Allergic Implications. II. Peripheral Circulatory Implications" – Vincent J. Fontana and Walter Redisch, New York University–Bellevue Medical Center, New York, N. Y.

ACTION OF NICOTINE AND SMOKING ON THE CORONARY CIRCULATION

Session Chairman: Carl J. Wiggers
Frank E. Bunts Educational Institute
Cleveland, Ohio

2:00 P.M. –

"The Physiology of the Coronary Circulation" – Donald E. Gregg, Walter Reed Army Institute of Research, Washington, D. C.

"Cardiac Effects of Intracoronary Arterial Injections of Nicotine in the Dog" – Samuel Bellet, James W. West, and Santiago V. Guzman, Philadelphia General Hospital, Philadelphia, Pa.

"Action of Nicotine and of Smoking on Coronary Circulation and Myocardial Oxygen Utilization" – Gerald Kien and Theodore R. Sherrod, University of Illinois College of Medicine, Chicago, Ill.

"Coronary Blood Flow and Cardiac Energetics During Pharmacodynamically Induced Increases in Left Ventricular Work: With Special Reference to the Effects of Nicotine, Hypertensin-II-Peptiden, Ethyl Alcohol, Epinephrine, and Norepinephrine" – Ivan E. Forte, A. Jane Williams, Louis Potgieter, J. E. Schmitthenner, J. H. Hafkenschiel, and Cecelia Riegel, The Lankenau Hospital, Philadelphia, Pa.

"Effect of Cigarette Smoking on Coronary Blood Flow and Myocardial Metabolism" – Richard J. Bing, Timothy Regan, and Harper Helms, Wayne State University College of Medicine, Detroit, Mich.

PANEL DISCUSSION

SIGNIFICANCE OF ELECTROCARDIOGRAPHIC AND BALLISTOCARDIOGRAPHIC CHANGES INDUCED BY SMOKING

Moderator: Isaac Starr
University of Pennsylvania School of Medicine
Philadelphia, Pa.

Discussants: Frank W. Davis, Jr., The Johns Hopkins University School of Medicine, Baltimore, Md.
Börje Ejrup, Karolinska Sjukhuset, Stockholm, Sweden.
John J. Kelly, Jr., Mercy Hospital, San Diego, Calif.

SATURDAY, MARCH 26, 1960

OTHER ASPECTS OF THE PHARMACOLOGY OF NICOTINE AND SMOKING

Session Chairman: McKeen Cattell
Cornell University Medical College
New York, N. Y.

9:00 A.M. –

"The Effects on Animals of Chronic Exposure to Tobacco Smoke" – Harvey B. Haag, Medical College of Virginia, Richmond, Va.

"The Chronic Effects of Nicotine" – Clinton H. Thienes, Institute of Medical Research, Huntington Memorial Hospital, Pasadena, Calif.

"The Effects of Nicotine and Cigarette Smoke on the Ballistocardiogram of the Dog" – Aldo N. Corbascio, University of California Medical Center, San Francisco, Calif., and James W. West, Philadelphia General Hospital, Philadelphia, Pa.

"Effect of Cigarette Smoking on the Intraocular Circulation" – Jerome W. Bettman and Victor Fellows, Stanford University School of Medicine, San Francisco, Calif.

"Effect of Cigarette Smoking and Intravenous Nicotine on Cerebral Blood Flow and Metabolism" – Richard L. Wechsler, Montefiore Hospital Institute of Research, Pittsburgh, Pa.

"Circulatory Responses to Smoking in Healthy Young Men" – Caroline Bedell Thomas, The Johns Hopkins University School of Medicine, Baltimore, Md.

"Comparison of Cardiovascular and Related Characteristics in Habitual Smokers and Non-Smokers" – Henry Blackburn, Josef Brozek, Henry L. Taylor, and Ancel Keys, University of Minnesota, Minneapolis, Minn.

EFFECTS OF NICOTINE AND SMOKING IN CARDIOVASCULAR DISORDERS

Session Chairman: Richard J. Bing
Wayne State University College of Medicine
Detroit, Mich.

2:00 P.M. –

"Cardiac Effects of Nicotine in the Rabbit with Experimental Coronary

Atherosclerosis" – Janet Travell, Seymour H. Rinzler, and Dorothy Karp, Cornell University Medical College, New York, N. Y.

"The Chronic Effects of Orally Administered Nicotine in Cholesterol-Fed Rabbits" – Duane G. Wenzel, University of Kansas School of Pharmacy, Lawrence, Kans., and James A. Turner, Veterans Administration Hospital, Kansas City, Mo.

"The Cardiovascular Effects of Smoking with Special Reference to Hypertension" – Grace M. Roth, Lovelace Clinic, Albuquerque, N. Mex.

"The Effects of Tobacco Smoke and Nicotine in Experimentally-Induced Coronary Deficiency" – Samuel Bellet, James W. West, Santiago V. Guzman, Otto Müller, and Antonio C. DeLeon, Philadelphia General Hospital, Philadelphia, Pa.

"Tobacco Allergy in Coronary Artery Disease" – Joseph Harkavy and Ely Pearlman, Mount Sinai Hospital, New York, N. Y.

PANEL DISCUSSION

EFFECTS OF SMOKING IN DISEASES
OF THE PERIPHERAL VASCULAR SYSTEM

Moderator: E. A. Hines, Jr.
Mayo Clinic
Rochester, Minn.

Discussants: Robert H. Goetz, Albert Einstein College of Medicine, New York, N. Y.
Hugh Montgomery, University of Pennsylvania School of Medicine, Philadelphia, Pa.
Grace M. Roth, Lovelace Clinic, Albuquerque, N. Mex.
J. Edwin Wood, Medical College of Georgia, Augusta, Ga.

Robert L. Kroc
Chairman

Charles Noback
Vice-Chairman

SECTION OF BIOLOGICAL AND MEDICAL SCIENCES

AND DIVISION OF MICROBIOLOGY

THE ACTINOMYCINS AND THEIR IMPORTANCE IN THE TREATMENT OF TUMORS IN ANIMALS AND MAN

Thursday, March 31, and
Friday, April 1, 1960

Conference Chairman: Selman A. Waksman
Institute of Microbiology, Rutgers, The State University
New Brunswick, N. J.

THURSDAY, MARCH 31, 1960

Session Chairman: Max Tishler
Merck Sharp & Dohme Research Laboratories
Rahway, N. J.

MICROBIOLOGICAL AND CHEMICAL

1:30 P.M. –
Greetings from the Academy – Robert L. Kroc, Chairman, Section of Biological and Medical Sciences, The New York Academy of Sciences, New York, N. Y.; Warner-Lambert Research Institute, Morris Plains, N. J.

Introductory Remarks – Selman A. Waksman, Institute of Microbiology, Rutgers, The State University, New Brunswick, N. J.

"Historical Background" – H. Boyd Woodruff, Merck Sharp & Dohme Research Laboratories, Rahway, N. J., and Selman A. Waksman, Institute of Microbiology, Rutgers, The State University, New Brunswick, N. J.

"The Production of Actinomycin by Directed Biosynthesis" – G. Schmidt-Kastner, Physiologischen Laboratorium, Farbenfabriken-Bayer, Leverkus, Germany.

"Biogenesis of the Actinomycins" – Edward Katz, Institute of Microbiology, Rutgers, The State University, New Brunswick, N. J.

"Structural Differences of the Actinomycins and Actinomycin Derivatives" – Hans Brockmann, University of Göttingen, Göttingen, Germany.

"Chemistry of Actinomycin D" – Alan W. Johnson, University of Nottingham, Nottingham, England.

"Mechanism of Action of Actinomycin D in Microbiological Systems" – Irving J. Slotnick, J. Hillis Miller Health Center, University of Florida, Gainesville, Fla.

8:00 P.M. –

"The Impact of Microbiology on Medicine and Public Health" – Selman A. Waksman, Institute of Microbiology, Rutgers, The State University, New Brunswick, N. J.

FRIDAY, APRIL 1, 1960

Session Chairman: C. Chester Stock
Sloan-Kettering Institute
New York, N. Y.

PHARMACOLOGY AND EXPERIMENTAL

9:00 A.M. –

"The Toxicity of Actinomycin D" – F. S. Philips, H. S. Schwartz, S. S. Stemberg, and Charlotte Tan, Sloan-Kettering Institute, New York, N. Y.

"Effect of Actinomycins Upon Experimental Tumors" – Chr. Hackmann, Hackmann, Institute for Experimental Pathology, Wuppertal-Elberfeld, Germany.

"Cytostatic Activity of Actinomycins in Mice" – Leonora Pugh, Institute of Microbiology, Rutgers, The State University, New Brunswick, N. J.

"Biological Studies on Actinomycin D" – Charlotte Maddock, Giulio D'Angio, Sidney Farber, and Alfred Handler, Children's Hospital Medical Center, Boston, Mass.

"Effect of Actinomycin Derivatives on Mouse Leukemia" – J. H. Burchenal, H. F. Oettgens, J. A. Reppert, and V. Coley, Sloan-Kettering Institute, New York, N. Y.

"Experimental Evaluation of Actinomycin D" – J. A. DiPaolo, Roswell Park Memorial Institute, Buffalo, N. Y.

Session Chairman: Stuart Sessoms
Cancer Chemotherapy National Service Center
Public Health Service
Bethesda, Md.

THE CLINICAL SIGNIFICANCE OF THE ACTINOMYCINS

2:00 P.M. –

"Clinical Studies of Actinomycin D" – Sidney Farber, Harvard Medical School and Children's Hospital Medical Center; Giulio D'Angio, Children's Hospital Medical Center; Audrey Evans and Anna Mitus, Children's Cancer Research Foundation, Boston, Mass.

"The Treatment of 200 Cases with Actinomycin D" – Joseph Burchenal and Charlotte Tan, Sloan-Kettering Institute, New York, N. Y.

"Clinical Studies of Actinomycin D" – George Moore, Roswell Park Memorial Institute, Buffalo, N. Y.

"Clinical Experience with Actinomycin C" – H. Begemann, Medizinische Universität Klinik, Freiburg im Breisgau, Germany.

"Clinical Applications and Methods of Administration of Actinomycin in the Treatment of Different Tumors" – A. Ravina and M. Pestel, Hôpital Beaujon, Clichy, France.

SECTION OF BIOLOGICAL AND MEDICAL SCIENCES

Robert L. Kroc
Chairman

Charles Noback
Vice-Chairman

DIVISION OF MICROBIOLOGY

Karl Maramorosch
Chairman

Emanuel Grunberg
Vice-Chairman

ORGANIZING COMMITTEE

Sidney Farber, Harvard Medical School, Boston, Mass.
George Moore, Roswell Park Memorial Institute, Buffalo, N. Y.
Stuart Sessoms, Cancer Chemotherapy National Service Center, Public Health Service, Bethesda, Md.
Max Tishler, Merck Sharp & Dohme Research Laboratories, Rahway, N. J.
Selman A. Waksman, Institute of Microbiology, Rutgers, The State University, New Brunswick, N. J.

NEW MEMBERS

Elected March 24, 1960

LIFE MEMBERSHIP

Beinfest, Sidney, Ph.D., Chemistry. Technical Vice-President, Berkeley Chemical Corporation, Berkeley Heights, N.J.

Sonneborn, Henry III, Ph.D., Petroleum Chemistry. Vice-President, Sonneborn Chemical and Refining Corporation. New York, N.Y.

SUSTAINING MEMBERSHIP

Bloom, Robert R., M.D., Bleeding Ulcers. Staff Member, Phelps Memorial Hospital, North Tarreytown, N.Y.

Gluesenkamp, Earl W., Ph.D., Industrial Research. Research Director, Monsanto Chemical Co., Dayton, Ohio.

Haller, Elden D., Ph.D., Chemistry & Chemical Engineering. Assistant to President, Arthur H. Thomas Company, Philadelphia, Pa.

Kenwell, Henry N., M.D., Basic and Applied Medical Research. Chairman, Department of Surgery, Millard Fillmore Hospital, Buffalo, N.Y.

ACTIVE MEMBERSHIP

Abbiss, Joseph William, M.D., Clinical Pathology. Director of Laboratories, The Memorial Hospital, Wilmington, Del.

Abbot, Ira H., B.S., Physical Sciences associated with Space Flight. Director, Advanced Research Programs, National Aeronautics and Space Administration, Chevy Chase, Md.

Abell, Paul I., Ph.D., Organic Chemistry. Associate Professor of Chemistry, University of Rhode Island, Kingston, R. I.

Abrahamson, Earl A., Ph.D., Analytical and Physical Chemistry. Assistant Division Supervisor, Physical and Analytical Division, E. I. du Pont de Nemours and Company, Wilmington, Del.

Ackerman, William Arnold, M.A., Petroleum and Colloidal Chemistry. Vice-President & Technical Director, Anderson Oil and Chemical Company Inc., Portland, Conn.

Adams, Harold Willard, Ph.D., Food Technology. Research Project Leader, Food Machinery and Chemical Corporation, San Jose, Calif.

Adams, John Quincy, M.D., Medical Science. Assistant Professor, Division of Obstetrics and Gynecology, University of Tennessee College of Medicine, Memphis, Tenn.

Adams, Phillip, Ph.D., Organic Synthesis. Assistant Director, Research and Development, Berkeley Chemical Corporation, Berkeley Heights, N.J.

Adams, William Hensley, Jr., Ph.D., Vertebrate ecology. Senior Game Biologist, Tennessee Game & Fish Commission, Madisonville, Tenn.

Adler, Fred P., Ph.D., Applied Physics. Director, Advanced Projects Laboratories, Hughes Aircraft Company, Culver City, Calif.

Adler, Richard H., M.D., Surgery. Assistant Professor Surgery, University of Buffalo, School of Medicine, Buffalo, N.Y.

Ahlquist, Raymond P., Ph.D., Pharmacology. Professor and Chairman, Medical College of Georgia, Augusta, Ga.

Aisenberg, Alan Clifford, Ph.D., Tumor Metabolism. Associate in Medicine, Harvard Medical School, Boston, Mass.

Aleksandrowicz, Julian, M.D., Hematology. Director, 3rd Clinic of Internal Diseases, University of Cracow, Poland.

Altman, Harold, M.D., Atherosclerosis. Resident in Pathology, E. W. Sparrow Hospital, Lansing, Mich.

Anderson, Merton B., M.D., Human Pathology. Assistant Professor of Pathology, Howard University College of Medicine, Washington, D.C.

Anderson, Patricia Rae, B.A., Medical Research. New York, N.Y.

Baker, Joseph J., M.D., Mental Health. Commissioner, Tennessee Department of Mental Health, Nashville, Tenn.

Bang, Edgar P., M.D., Medicine and Surgery. Private Practice, Glen Cove, N.Y.

Benbow, Robert H., M.D., Obstetrics-Gynecology. Private Practice, Bryan, Texas.

Bentman, J. J., D.D.S., Periodontology. Associate in Oral Medicine, University of Pennsylvania Graduate School of Medicine, Philadelphia, Pa.

Beredjick, Nicky, Ph.D., Polymer Chemistry. Assistant Project Chemist, Standard Oil Company, Whiting, Ind.

Blattner, Russell J., M.D., Pediatrics. Professor and Chairman, Baylor University College of Medicine, Houston, Texas.

Blicharski, Julian, M.D., Hematology. Rockefeller Foundation Fellow, M. D. Anderson Hospital and Tumor Institute, Houston, Texas.

Bodman, John, M.D., Chemical Pathology of Cancer. Royal Hospital, Richmond, Surrey, England.

Borowsky, Melvin, M.D., Pathology. Resident in Pathology, National Naval Medical Center, Bethesda, Md.

Boyle, John E. Whiteford, Ph.B., History of Science. Director, American Friends of The Middle East, Tehran, Iran.

Breneman, W. R., Ph.D., Endocrinology. Professor of Zoology, Indiana University, Bloomington, Ind.

Brenizer, Addison Gorgas, Jr., M.D., Surgery. Chief, Surgical Service, Charlotte Memorial Hospital, Charlotte, N.C.

Brinson, John B., Jr., M.D., Medicine. Private Practice, Madison, Fla.

Bucci, Luigi, M.D., Pharmacology applied to Psychiatry. Senior Resident, Rockland State Hospital, Orangeburg, N.Y.

Cady, Lee D., Jr., M.D., Cardiovascular Epidemiology. Special Research Fellow, U.S. Public Health Service, New York, N.Y.

Canfield, Richard G., M.D., Internal Medicine. Instructor, University of Pittsburgh Pittsburgh, Pa.

Carmichael, Oliver C., Jr., Ph.D., Education. President, Converse College, Spartansburg, S.C.

Cash, William D., Ph.D., Peptide and Protein Hormones. Assistant Professor of Biochemistry, Cornell University Medical College, New York, N.Y.

Chazen, Eric Martin, M.D., Pediatrics. Senior Resident Pediatrician, Children's Hospital, Boston, Mass.

Cheydleur, Eleanor Payne, M.D., Gynecology. Private Practice, Evansville, Ind.

Ciferri, Raffaele M., Ph.D., Pure and Applied Mycology. Director, Botanical Institute, The University, Pavia, Italy.

Clark, Wallace Henderson, Jr., M.D., Electron Microscopy. Associate Professor of Pathology, Tulane University, New Orleans, La.

Coler, Myron A., Ph.D., Research Methods. Technical Director, Markite Co., New York, N.Y.

Colvell, Betty Anne, Microbiology. Assistant Scientist, Warner-Lambert Research Institute, Morris Plains, N.J.

Corday, Emy V., B.A., Hair and Scalp Therapy. Private Practice, New York, N.Y.

Cowley, Clement W., B.S., Low Temperature Preservation of Biological Materials. Research Engineer, The Linde Company, Tonawanda, N.Y.

Cyr, Donat P., M.D., Internal Medicine. Private Practice, Boston, Mass.

Deinhardt, Friedrich, M.D., Microbiology. Assistant Professor, Department of Public Health and Preventive Medicine, University of Pennsylvania School of Medicine, Philadelphia, Pa.

Delahunt, Charles S., D.V.M., Toxicology. Manager, Toxicology Section, Charles Pfizer & Company Inc., Groton, Conn.

De Schepper, Paul J., M.D., Internal Medicine. Post-Graduate Research Fellow in Neurobiochemistry (Fullbright Exchange Fellow from Belgium) Baltimore, Md.

Devlin, William J., Ph.D., Psychiatry. Clinical Instructor Neurology and Psychiatry, Loyola University, Chicago, Ill.

Dick, Lionel A., M.D., Dermatology. Clinical Instructor, New York University Post Graduate Medical School, New York, N.Y.

Doyle, Lee Lee, B.A., Reproductive Physiology. Research Assistant, Stanford University School of Medicine, Stanford Medical Center, Palo Alto, Calif.

Eigelsbach, Henry T., Ph.D., Medical Bacteriology. Supervisory Bacteriologist and Chief, Medical Bacteriology Division, Fort Detrick, Md.

Elliot, Alfred M., Ph.D., Protozoology. Professor of Zoology, University of Michigan, Ann Arbor, Mich.

Fabi, Mario N., M.D., Internal Medicine. Chief of Medicine, Scranton State Hospital, Scranton, Pa.

Failey, Crawford Fairbanks, Ph.D., Biochemistry. Retired, Terre Haute, Ind.

Fairbanks, Richard Henry, Sr., M.S., Organic (steroid) Chemistry. Instructor of Urology, Post-Graduate Medical School, Bellevue Medical Center, New York, N.Y.

Farinacci, Nicholas T., Ph.D., Steroid Hormones. Owner and Director of Scien-Tech, New York, N.Y.

Fasman, Gerald D., Ph.D., Proteins. Assistant Head, Biophysical Chemistry, Children's Cancer Research Foundation, Boston, Mass.

Favorite, John R., B.S., Graphic Arts. Technical Director, Minnesota Mining & Manufacturing Company, St. Paul, Minn.

Feldman, Sanford E., M.D., Nutritional Physiology. Associate Research Surgery, Poultry Department, University of California, San Francisco, Calif.

Ferrari, William, Phar.D., Direttore inc. Instituto di Farmacologia Universita di Cagliari, Cagliari, Italy.

Fishel, Leo, Jr., M.D., Internal Medicine. Private Practice, Freeport, N.Y.

Flotte, C. Thomas, M.D., Surgery. Assistant Professor of Surgery, University of Maryland, Baltimore, Md.

Foster, Giraud Vernam, M.D., Endocrinology. Senior Assistant Resident in Medicine, University Hospital, Baltimore, Md.

Fudema, John J., M.S., Neuro-pharmacology. Research Fellow in Neuropediatrics, Cook County Hospital, Chicago, Ill.

Fuentes, Cesar A., M.D., Medical Mycology. Professor, Experimental Pathology. Universidad de La Habana, Habana, Cuba.

Gaboury, M. N., B.S., Manufacture. Manager, Organic Chemicals Division, American Cyanamid Company, Bound Brook, N.J.

Gagne, Joseph, Phm.D., Pharmacy. Professor of Pharmacy, Hampden College, Willimansett, Mass.

Galton, Michael, D.Obst., Obstetrics. Research Fellow in Pathology, Free Hospital for Women, Harvard Medical School, Brookline, Mass.

Gantt, Clarence L., M.D., Endocrinology. Clinical Instructor in Medicine,

University of Illinois School of Medicine, Evanston, Ill.

Geiger, Hugh S. Jr., M.D., General Medicine. Private Practice, East Point, Ga.

Geller, Leonard, Ph.D., Mathematics. Lacquer & Chemical Corporation, New York, N.Y.

Gentry, Thomas Christy, M.D., Preventive Medicine. Regional Flight Surgeon, Federal Aviation Agency, Jamaica, N.Y.

Giles, Robert B., Jr., M.D., Metabolism of Hexosamines and Glycoproteins. Clinical Assistant Professor of Internal Medicine, University of Texas Southwestern Medical School, Dallas, Tex.

Gilman, Carl J., M.D., Urology. Private Practice, Boulder, Colo.

Glass, Laurel Ellen, Ph.D., Experimental Embryology. Instructor in Anatomy, University of California Medical School, San Francisco, Calif.

Glassy, Frank J., M.D., Pathology. Director of Laboratories, Saint Joseph's Hospital, Marshfield, Wisc.

Goldemberg, Robert L., B.S., Cosmetics. Director, Toiletries Research, Shulton Inc., Clifton, N.J.

Gosselin, Robert E., Ph.D., Pharmacology. Professor of Pharmacology, Dartmouth Medical School, Hanover, N.H.

Goswitz, Francis Andrew, M.D., Internal Medicine. Internist, U. S. Army, Fort Campbell, Ky.

Green, Martin A., M.D., Medicine. Attending-in-Charge, Neurology-Electroencephalograpy, North Shore Hospital, Manhasset, N.Y.

Guidotti, Guido, M.D., Carbohydrate and Protein Metabolism. Research Fellow in Physiology, Chicago Medical School, Chicago, Ill.

Hance, Anthony James, Ph.D., Neuropharmacology. Assistant Research Pharma- University of California Medical Center, Los Angeles, Calif.

Handler, Eugene S., M.S., Hematology. Research Assistant, New York University, New York, N.Y.

Harrat, Frank Turner, M.D., Medicine and Surgery. Chief of Staff, Miner's Hospital, Frostburg, Md.

Hayashi, Hajime, M.S., Virology and Immunology. Graduate Research Assistant, Michigan State University, East Lansing, Mich.

Hirschberg, Sidney, Pod.D., Podiatry. President, Board of Trustees, American Foot Health Foundation, New York, N.Y.

Holleb, Arthur I., M.D., Surgical Treatment of Cancer. Assistant Attending Surgeon, Breast Service, Memorial Center, New York, N.Y.

Holliday, Audrey R., Ph.D., Psychopharmacology. Research Assistant Professor, University of Washington, Seattle, Wash.

Horvitz, Samuel, A.B., Physics. President, Decisions, Inc., Fall River, Mass.

Hudell, John Carl, M.D., Internal Medicine. Private Practice, Aurora, Ill.

Ito, Canada, M.D., Medical Science. Scientific Coordinator, Cyanamid International, Osada, Japan.

Ito, Yosoji, Ph.D., Biochemistry. Professor, The University of Tokyo, Tokyo, Japan.

Jaffe, A. J., Ph.D., Manpower and Population. Director, Manpower and Population Program, Bureau of Applied Social Research, Columbia University, New York, N.Y.

Jenny, Jacques, D.V.M., Orthopedic Surgery. Associate Professor of Surgery, School of Veterinary Medicine, University of Pennsylvania, Philadelphia, Pa.

Johnson, John, M.T., Medical Sciences. Laboratory Supervisor, Diagnostic Laboratories Miami Valley Hospital, Dayton, Ohio.

Jonsson, Ake, Technical Director, Medicinal Chemistry. Associate Director of Research, Sodertalje, Sweden.

Kafig, Emanuel, Medical Research. Physical Science Technician, Naval Medical

Research Institute, Bethesda, Md.

Kato, Kyuichi, M.D., Pharmacology. Assistant in the Pharmacology Department, University of Milano, Milano, Italy.

Katzenstein, Rolf E., M.D., Pathology. Director of Laboratories, Meriden Hospital, Meriden, Conn.

Kaufman, I. Charles, M.D., Behavioral Psychiatry. Associate Professor of Psychiatry, Boston University School of Medicine, Boston, Mass.

Kawase, Osamu, M.D., Biology and Medicine. Professor in Pathology, Kumamoto University, Kumamoto, Japan.

Kaye, Abraham, M.D., Psychiatry. Private Practice, Farmingham, Mass.

Keyes, Margaret Jeanne, B.A., Psychology. M.C.A., New York, N.Y.

Kimbrough, Raymond Devan, Jr., Ph.D., Biochemistry-Organic Chemistry. Research Associate, Cornell University Medical College, New York, N.Y.

Klotz, L. J., Ph.D., Hematology. Director of Research, Cincinnati, Ohio.

Korein, Julius, M.D., Neurology. Assistant Clinical Instructor in Neurology. Bellevue Hospital, New York University - Bellevue Medical Center, New York, N.Y.

Kraft, George L., M.D., Orthopedics. Practising Orthopedic Surgeon, North Hollywood, Calif.

Kramer, Bernard, Inc., M.D., Metabolism of Drugs. Research Investigator, Army Clinical Center, Md.

Krinsley, David H., Ph.D., Geology. Instructor in Geology, Queens College, Flushing, N.Y.

Kuwabara, Seishi, D.Sc., Biology. Professor of Biological Chemistry, Shimonoseki College of Fisheries, Shimonoseki City, Japan.

Lamesta, Lidia, M.D., Psychopharmacology. Assistant of Institute of Pharmacology, University of Milano, Milano, Italy.

Lanzano, Gaetano, Doctor in Engineering, Nuclear Engineering. Representative, National Committee for Nuclear Researches of Italy, Washington, D.C.

Lavelle, Sean, M.D., Hematology. Professor and Chairman, Department of Experimental Medicine, University College, Galway, Ireland.

Leander, Richard Benjamin, M.D., Neuro-Psychiatry. Private Practice, Sioux Falls, S.D.

Leblond, C. P., Ph.D., Radioautography. Professor of Anatomy, McGill University, Montreal, Canada.

Lefebvre, Marcel, B.S., Bacteriology. Medical Bacteriologist, Maisonneuve Hospital and Institute of Cardiology of Montreal, Montreal, Canada.

Lewinter, Paul, M.D., Gastroenterology. Captain, U. S. Army Hospital, Fort Campbell, Ky.

Liberatore, Giacomo, B.S., Protozoology. Teaching Fellow at New York University, New York, N.Y.

Liebersohn, Aron, M.S., Research in Transients of the Electric Motor Drive. Municipal Engineer. New York City Transit Authority, Brooklyn, N.Y.

Livingston, Philip Henry, M.D., Cardiovascular Diseases. Cardiologist, Erlanger Memorial Childrens Hospitals, Chattanooga, Tenn.

Longworth, Ruskin, Ph.D., Physical Polymer Chemistry. Research Chemist, E. I. du Pont de Nemours and Company, Wilmington, Del.

Lumb, George Dennett, M.D., Pathology. Director of Laboratories, James Walker Hospital, Washington, D.C.

McCoy, Richard H., Ph.D., Biochemistry. Professor of Chemistry, Division of the Natural Sciences, University of Pittsburgh, Pittsburgh, Pa.

McKay, Kenneth G., D.V.M., Veterinary Medicine. Extension Veterinarian, University of California, Davis, Calif.

MacKenzie, W. B., B.S., Electrical Insulation, Chief Chemist, Phelps Dodge

Copper Products Corporation, Yonkers, N.Y.

Mahl, Murray Martin, M.D., Medicine. Clinical Instructor in Medicine, New York Medical College, New York, N.Y.

Manaresi, Alberto, M.D., Internal Medicine. Assistant at Clinica Medica, University of Bologna, Bologna, Italy.

Marshall, C. Edmund, Ph.D., Soil Science. Professor of Soils, University of Missouri, Columbia, Mo.

Mathews, William R., M.D., Pathology. Pathologist, Confederate Memorial Medical Center, Shreveport, La.

Maumenee, A. Edward, M.D., Ophthalmology. Director, Wilmer Ophthalmological Institute, Johns Hopkins Hopsital, Baltimore, Md.

Meloy, Thomas, S.B., Physics. President, Melpar, Inc., Falls Church, Va.

Menustik, John, Jr., M.D., Anesthesiology. Attending Anesthesiologist, Champlain Valley Hospital and Physicians Hospital, Plattsburgh, N.Y.

Meredith, Jesse Hedgepeth, M.D., Surgery. Director of Surgical Research, Bowman Gray School of Medicine, Winston-Salem, N.C.

Merrill, Joseph M., M.D., Clinical Physiology. Instructor of Medicine, Vanderbilt University School of Medicine, Nashville, Tenn.

Metzgar, Richard S., Ph.D., Immunology. Cancer Research Scientist, Roswell Park Memorial Institute, Buffalo, N.Y.

Miedler, Leo J., M.D., Environmental Dermatology. Research Associate and Instructor Department of Dermatology, University of Michigan, Ann Arbor, Mich.

Miller, Katherine Sue, M.S., Pharmacology. Scientist, E. R. Squibb & Sons, New Brunswick, N.J.

Mosley, James Wilson, M.D., Epidemiology. Chief, Hepatitis Unit, Communicable Disease Center, Public Health Service, Boston, Mass.

Nakabayash, Nicholas T., Ph.D., Reproductive Physiology. Junior Research Physiologist, Department of Surgery, UCLA Medical Center, Los Angeles, Calif.

Neary, E. P., M.D., Medicine. Private Practice, Cleveland, Ohio.

Nemeth, Burton, D.Ch., Physiology. Librarian, Chiropractic Institute of New York, Brooklyn, N.Y.

Nichols, Florence B., M.S., Psychology. Psychodiagonostic Testing, New York University College of Medicine, New York, N.Y.

Noell, Werner K., M.D., Neurophysiology. Associate Professor, University of Buffalo School of Medicine, Buffalo, N.Y.

Nunnemacher, Rudolph F., Ph.D., Zoology. Professor of Biology, Clark University, Worcester, Mass.

Oom, Bengt, D.Chem.Eng., Pharmaceutical and Medicinal Chemistry. Vice-President in Charge of Research, Development and Control, A.B. Astra, Sodertalje, Sweden.

Ordonez-Plaja, Antonio, M.D., Surgery. Assistant Professor in Surgery, National University School of Medicine, Bogota, Colombia.

Orfila, Jeanne, M.D., Immunology. Laboratory Chief, Laboratorie de Bacteriologie, Faculté de Medecine, Alger, Algeria.

Orsino, Joseph A., Ph.D., Organic Chemicals. Technical Director, National Lead Company Laboratories, Brooklyn, N.Y.

Oster, Irwin I., Ph.D., Genetics. Assistant Member, Division of Chemotherapy, The Institute for Cancer Research, Philadelphia, Pa.

Pembleton, Williams Edwin, M.D., Medical Sciences. Professor of Anesthesiology, Medical College of Virginia, Richmond, Va.

Perkin, Harold J., M.A., Clinical Laboratory. Director, Lahey Clinic, Boston, Mass.

Perrin, James M., M.A., Reference Librarian. Assistant Professor, College of

the Pacific, Stockton, Calif.

Prescott, George C., M.A., Analytical Chemistry. Chemist, The Upjohn Company, Kalamazoo, Mich.

Proescher, Frederick, M.D., Pathology. Private Practice, San Jose, Calif.

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NOTICE TO ACTIVE MEMBERS

In accordance with the Bylaws of the Academy, Article VIII, Section 5, the Nominating Committee of the Council is inserting in this April issue a notice to Active Members, quoting Article V, Section 1 of the Bylaws.

Article V, Section 1 reads as follows:

"**Suggestions by the Members for Nominations.** Suggestions for nominations of Officers of the Academy and Members of the Board of Trustees and of the Scientific Council may be sent in writing by any Active Member of the Academy, addressed to the Recording Secretary, with the name of the Member offering such suggestion. To be considered, such suggestions must be received not later than September 1 of each year."